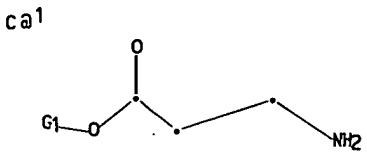
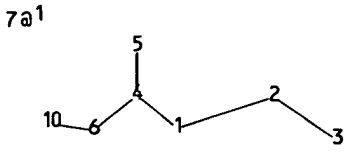
L Number	Hits	Search Text	DB	Time stamp
1	933	((514/567) or (562/576)).CCLS.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/12/29 06:11
2	1879069	2003.py.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/12/29 06:11
3	155	(((514/567) or (562/576)).CCLS.) and 2003.py.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/12/29 06:11

C:\STNEXP4\QUERIES\09932677 (anion-carboxy).str



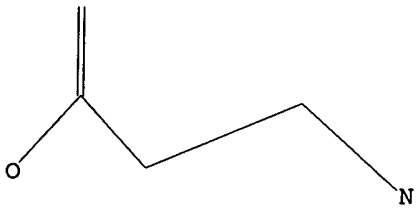


chain nodes :
1 2 4 5 6 10
ring/chain nodes :
3 7
chain bonds :
1-2 1-4 2-3 4-5 4-6 6-10
exact/norm bonds :
2-3 4-5 4-6 6-10
exact bonds :
1-2 1-4

G1:H,[*1]

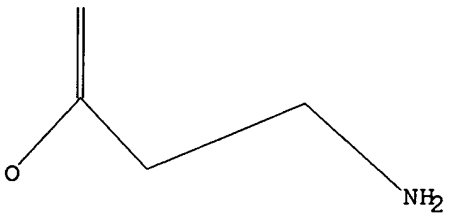
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 10:CLASS

```
=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2026 OR  2039 OR  2045 OR  2046 OR  2047

L1    SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\09932677 (anion-carboxy).str

L2      STRUCTURE UPLOADED

=> que L2 NOT L1

L3   QUE L2 NOT L1

=> d l3
L3 HAS NO ANSWERS
L1              SCR 2026 OR 2039 OR 2045 OR 2046 OR 2047
L2              STR
```



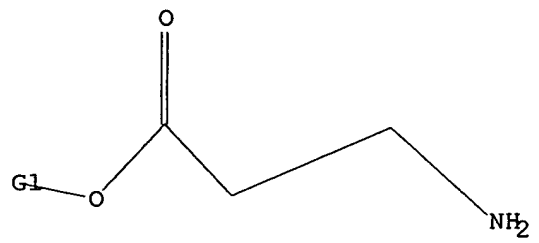

```
Structure attributes must be viewed using STN Express query preparation.
L3              QUE  L2 NOT L1


=> s l3 sss sam
SAMPLE SEARCH INITIATED 16:47:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  41376 TO ITERATE

  2.4% PROCESSED    1000 ITERATIONS                                 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       815422 TO   839618
PROJECTED ANSWERS:          304506 TO   319444

L4          50 SEA SSS SAM L2 NOT L1

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2026 OR  2039 OR  2045 OR  2046 OR  2047
```

```
L5    SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\09932677 (anion-carboxy).str

L6      STRUCTURE UPLOADED

=> que L6 NOT L5

L7   QUE L6 NOT L5

=> d l7
L7 HAS NO ANSWERS
L5              SCR 2026 OR 2039 OR 2045 OR 2046 OR 2047
L6              STR
```




```
Structure attributes must be viewed using STN Express query preparation.
L7              QUE  L6 NOT L5


=> s l7 sss sam
SAMPLE SEARCH INITIATED 16:48:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  41376 TO ITERATE

  2.4% PROCESSED    1000 ITERATIONS                              24 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       815422 TO   839618
PROJECTED ANSWERS:           17970 TO    21750

L8          24 SEA SSS SAM L6 NOT L5

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2026 OR  2039 OR  2045 OR  2046 OR  2047

L9    SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\09932677 (anion-carboxy).str

L10     STRUCTURE UPLOADED
```

```
=> que L10 NOT L9

L11  QUE L10 NOT L9

=> d l11
L11 HAS NO ANSWERS
L9              SCR 2026 OR 2039 OR 2045 OR 2046 OR 2047
L10             STR

  1
```




```
G1 H,[@1]


Structure attributes must be viewed using STN Express query preparation.
L11             QUE  L10 NOT L9


=> s l11 sss sam
SAMPLE SEARCH INITIATED 16:50:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  41376 TO ITERATE

  2.4% PROCESSED    1000 ITERATIONS                              24 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       815422 TO   839618
PROJECTED ANSWERS:           17970 TO    21750

L12          24 SEA SSS SAM L10 NOT L9

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 1568

L13   SCREEN CREATED

=> screen 2026 OR  2039 OR  2045 OR  2046 OR  2047

L14   SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\09932677 (anion-carboxy).str
```

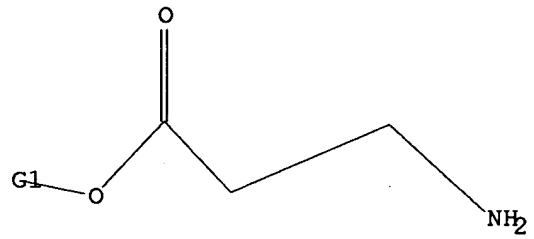
L15 STRUCTURE UPLOADED

=> que L15 AND L13 NOT L14

L16 QUE L15 AND L13 NOT L14

=> d l16
L16 HAS NO ANSWERS
L13 SCR 1568
L14 SCR 2026 OR 2039 OR 2045 OR 2046 OR 2047
L15 STR

1



G1 H,[@1]

Structure attributes must be viewed using STN Express query preparation.
L16 QUE L15 AND L13 NOT L14

=> s l16 sss sam
SAMPLE SEARCH INITIATED 16:51:41 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 19967 TO ITERATE

5.0% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 390898 TO 407782
PROJECTED ANSWERS: 31473 TO 36413

L17 50 SEA SSS SAM L15 AND L13 NOT L14

=> s l16 sss ful
FULL SEARCH INITIATED 16:53:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 401237 TO ITERATE

99.7% PROCESSED 400000 ITERATIONS 29852 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.07

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 401237 TO 401237
PROJECTED ANSWERS: 29852 TO 30462

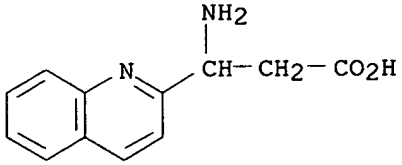
```
L18       29852 SEA SSS FUL L15 AND L13 NOT L14

=> s l18
L19       28144 L18

=> s epilepto?
L20        1917 EPILEPTO?

=> s l19 and l20
L21           8 L19 AND L20

=> d l21 1-8 bib,ab,hitstr
```

L21 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:927248 CAPLUS
DN 138:4513
TI Preparation of heterocyclic .beta.-amino acids as antiepileptogenic agents
IN Campbell, Allyson J.; Weaver, Donald F.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

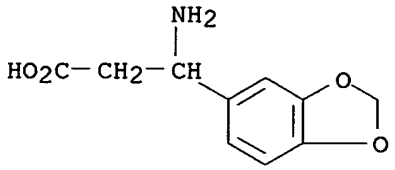
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002096424	A1	20021205	WO 2002-CA773	20020527

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

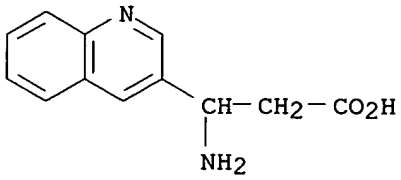
PRAI US 2001-293495P P 20010525
OS MARPAT 138:4513
AB Heterocyclic .beta.-amino acids are claimed for the prevention or treatment of **epileptogenesis**-assocd. diseases. Representative heterocyclic moieties are the following: thienyl, pyrrolyl, pyrimidyl, pyrazinyl, pyrazolyl, oxazolyl, isooxazolyl, thiazolyl, isothiazolyl, imidazolyl, furanyl, benzothiazolonyl, indolonyl, benzooxoazolinyl, benzothiophenyl, benzofuranyl, quinolinyl, isoquinolinyl, benzodioxazolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, methylenedioxyphenyl, ethylenedioxyphenyl, indolyl, purinyl, and deazapurinyl. Thus, 3-amino-3-(benzo[d]-1,3-dioxolan-5-yl)propionic acid was prepd. by condensation of benzo[d]-1,3-dioxolane-5-carboxaldehyde with malonic acid and ammonium acetate.
IT **100142-82-3P 129042-60-0P 129042-67-7P 138621-63-3P 339994-86-4P 477250-29-6P 477250-44-5P 477250-45-6P 477250-46-7P 477250-47-8P 477250-48-9P 477250-49-0P 477250-50-3P 477250-51-4P 477250-52-5P 477250-53-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic .beta.-amino acids as antiepileptogenic agents)
RN 100142-82-3 CAPLUS
CN 2-Quinolinepropanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



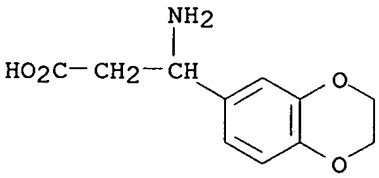
RN 129042-60-0 CAPLUS
CN 1,3-Benzodioxole-5-propanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



RN 129042-67-7 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)

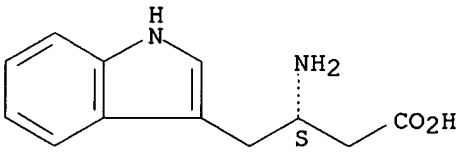


RN 138621-63-3 CAPLUS
CN 1,4-Benzodioxin-6-propanoic acid, .beta.-amino-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 339994-86-4 CAPLUS
CN 1H-Indole-3-butanoic acid, .beta.-amino-, monohydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

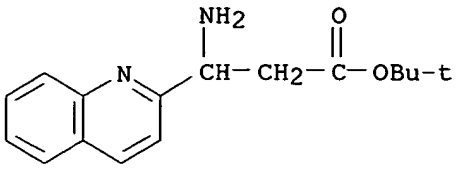
Absolute stereochemistry.



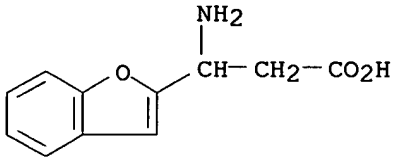
● HCl

RN 477250-29-6 CAPLUS
CN 2-Quinolinepropanoic acid, .beta.-amino-, 1,1-dimethylethyl ester (9CI)

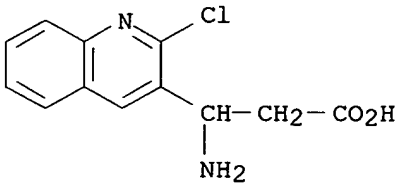
(CA INDEX NAME)



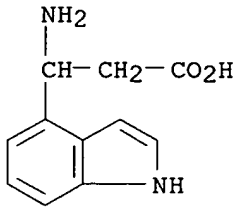
RN 477250-44-5 CAPLUS
CN 2-Benzofuranpropanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



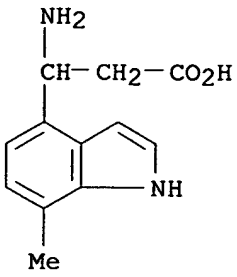
RN 477250-45-6 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-amino-2-chloro- (9CI) (CA INDEX NAME)



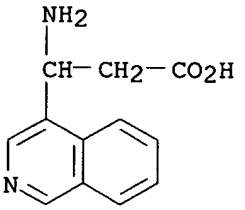
RN 477250-46-7 CAPLUS
CN 1H-Indole-4-propanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



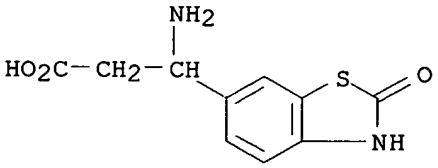
RN 477250-47-8 CAPLUS
CN 1H-Indole-4-propanoic acid, .beta.-amino-7-methyl- (9CI) (CA INDEX NAME)



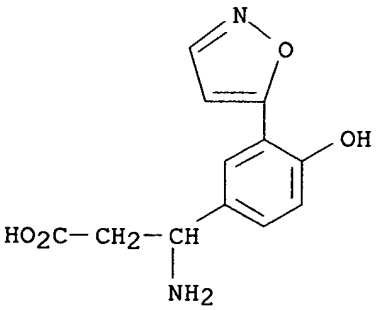
RN 477250-48-9 CAPLUS
CN 4-Isoquinolinepropanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



RN 477250-49-0 CAPLUS
CN 6-Benzothiazolepropanoic acid, .beta.-amino-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



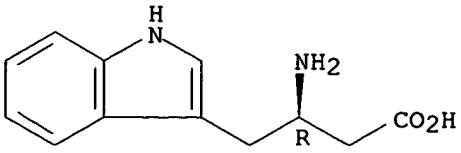
RN 477250-50-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-hydroxy-3-(5-isoxazolyl)- (9CI) (CA INDEX NAME)



RN 477250-51-4 CAPLUS

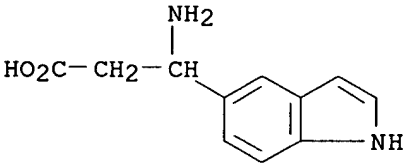
CN 1H-Indole-3-butanoic acid, .beta.-amino-, monohydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

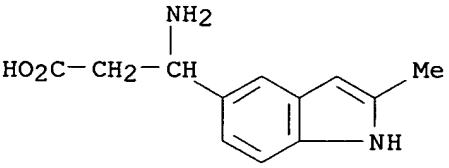


● HCl

RN 477250-52-5 CAPLUS
CN 1H-Indole-5-propanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



RN 477250-53-6 CAPLUS
CN 1H-Indole-5-propanoic acid, .beta.-amino-2-methyl- (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:716608 CAPLUS
DN 137:242191
TI Antiepileptogenic agents
IN Weaver, Donald F.; Tan, Christopher Y. K.; Kim, Stephen T.; Kong, Xianqi; Wei, Lan; Carran, John R.
PA Queen's University at Kingston, Can.; Neurochem Inc.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English

not prior !

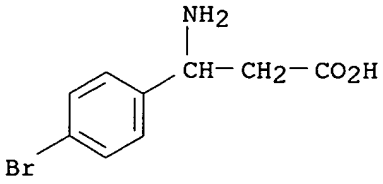
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002073208	A2	20020919	WO 2002-CA363	20020313

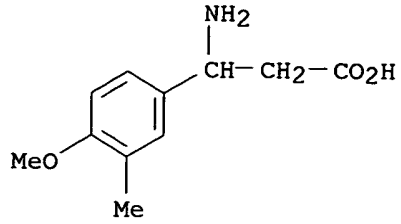
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

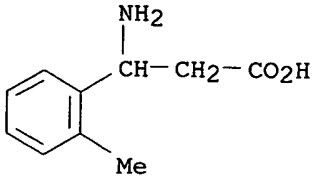
PRAI US 2001-275618P P 20010313
OS MARPAT 137:242191
AB The invention discloses methods and compds. useful for the treatment of convulsive disorders, including epilepsy. The methods and compds. of the invention inhibit or prevent ictogenesis and/or **epileptogenesis**. The invention also discloses methods for prepg. these anticonvulsant compds.
IT **39773-47-2P 54503-17-2P 68208-16-2P 68208-17-3P 213192-51-9P 213192-54-2P 213192-60-0P 213192-66-6P 460039-53-6P 460039-54-7P 460039-55-8P 460039-56-9P 460039-57-0P 460039-58-1P 460039-59-2P 460039-61-6P 460039-62-7P 460039-63-8P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-**epileptogenic** agents)
RN 39773-47-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-bromo- (9CI) (CA INDEX NAME)



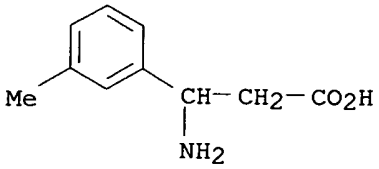
RN 54503-17-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methoxy-3-methyl- (9CI) (CA INDEX NAME)



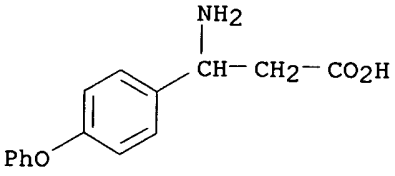
RN 68208-16-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-methyl- (9CI) (CA INDEX NAME)



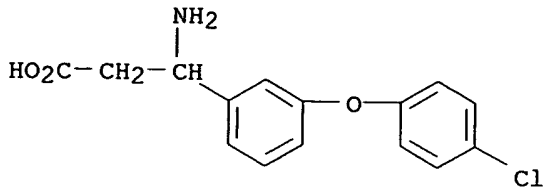
RN 68208-17-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-methyl- (9CI) (CA INDEX NAME)



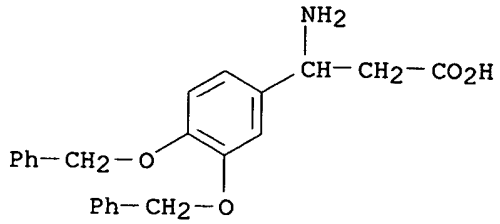
RN 213192-51-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-phenoxy- (9CI) (CA INDEX NAME)



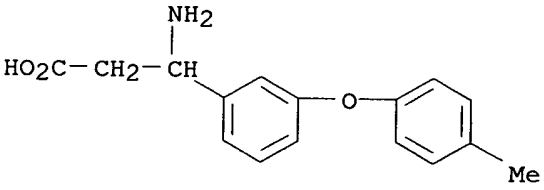
RN 213192-54-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-chlorophenoxy)- (9CI) (CA INDEX NAME)



RN 213192-60-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3,4-bis(phenylmethoxy)- (9CI) (CA INDEX NAME)

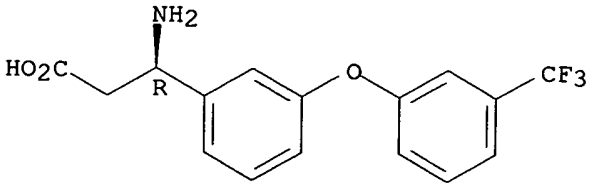


RN 213192-66-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)- (9CI) (CA INDEX NAME)



RN 460039-53-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]-, hydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

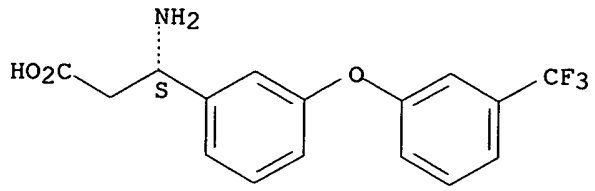
Absolute stereochemistry.



● HCl

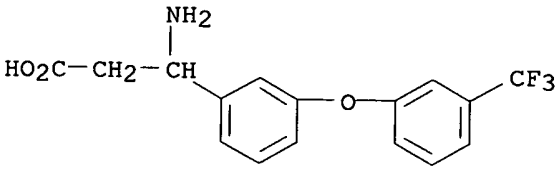
RN 460039-54-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]-, hydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

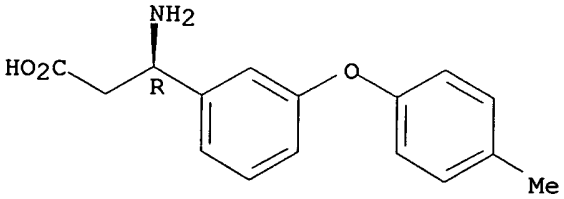
RN 460039-55-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 460039-56-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)-, hydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

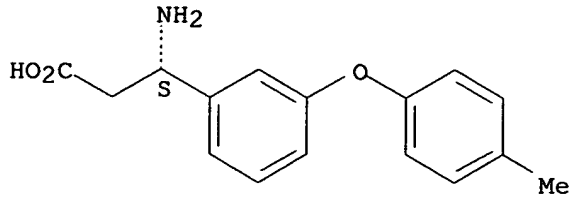
Absolute stereochemistry.



● HCl

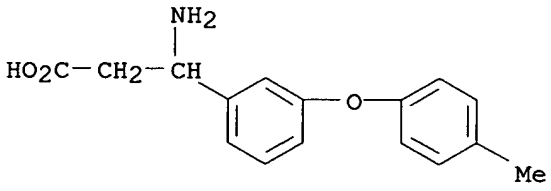
RN 460039-57-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)-, hydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

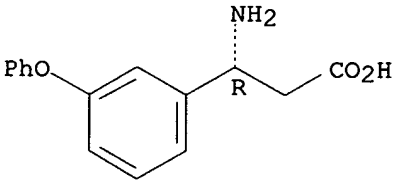
RN 460039-58-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 460039-59-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy-, hydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

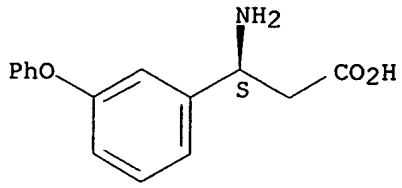
Absolute stereochemistry.



● HCl

RN 460039-61-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy-, hydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

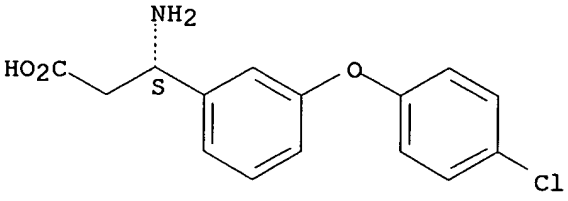
Absolute stereochemistry.



● HCl

RN 460039-62-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-chlorophenoxy)-, hydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

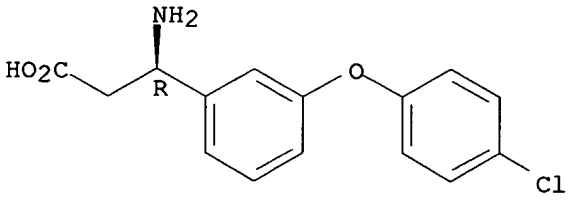
Absolute stereochemistry.



● HCl

RN 460039-63-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-chlorophenoxy)-, hydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

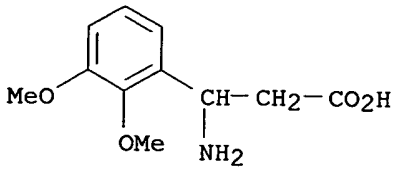


● HCl

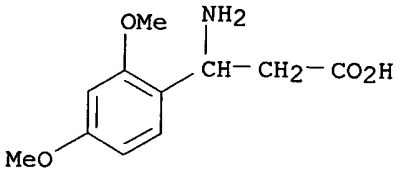
IT **34840-98-7 34841-02-6 68208-18-4**
80971-95-5 102308-62-3 129042-81-5
180263-44-9 213192-58-6 282524-82-7
299165-24-5 412925-58-7 460039-36-5
460039-37-6 460039-38-7 460039-39-8
460039-42-3 460039-43-4 460039-44-5

460039-45-6 460039-60-5
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**epileptogenic** agents)

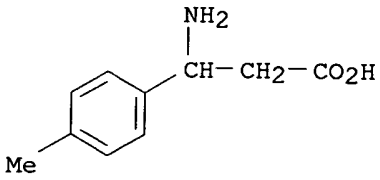
RN 34840-98-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2,3-dimethoxy- (9CI) (CA INDEX NAME)



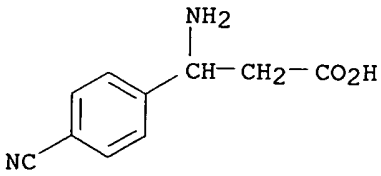
RN 34841-02-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2,4-dimethoxy- (9CI) (CA INDEX NAME)



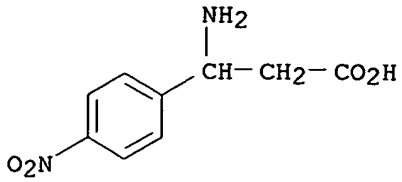
RN 68208-18-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methyl- (9CI) (CA INDEX NAME)



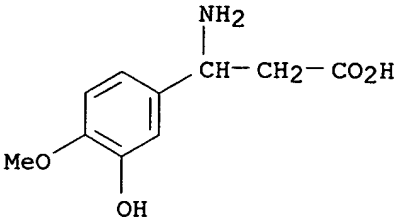
RN 80971-95-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-cyano- (9CI) (CA INDEX NAME)



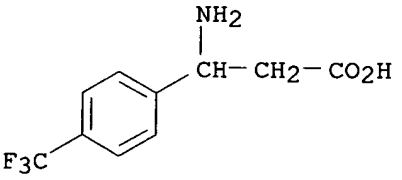
RN 102308-62-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-nitro- (9CI) (CA INDEX NAME)



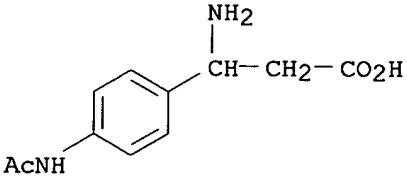
RN 129042-81-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-hydroxy-4-methoxy- (9CI) (CA INDEX NAME)



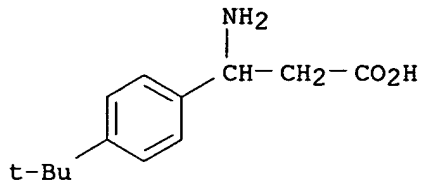
RN 180263-44-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



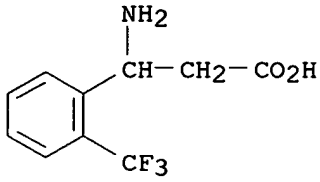
RN 213192-58-6 CAPLUS
CN Benzenepropanoic acid, 4-(acetylamino)-.beta.-amino- (9CI) (CA INDEX NAME)



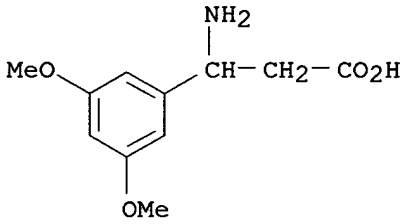
RN 282524-82-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



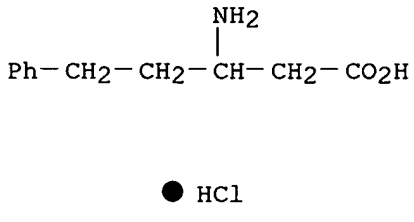
RN 299165-24-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



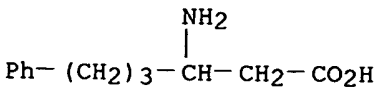
RN 412925-58-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3,5-dimethoxy- (9CI) (CA INDEX NAME)



RN 460039-36-5 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-, hydrochloride (9CI) (CA INDEX NAME)

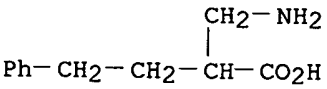


RN 460039-37-6 CAPLUS
CN Benzenehexanoic acid, .beta.-amino-, hydrochloride (9CI) (CA INDEX NAME)



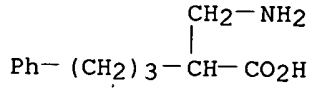
● HCl

RN 460039-38-7 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



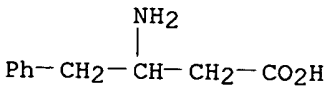
● HCl

RN 460039-39-8 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



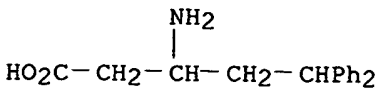
● HCl

RN 460039-42-3 CAPLUS
CN Benzenebutanoic acid, .beta.-amino-, hydrochloride (9CI) (CA INDEX NAME)



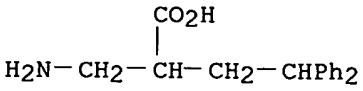
● HCl

RN 460039-43-4 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-.delta.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



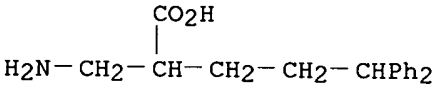
● HCl

RN 460039-44-5 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-.gamma.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



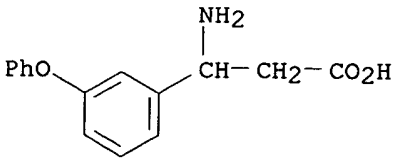
● HCl

RN 460039-45-6 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-.delta.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 460039-60-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy-, hydrochloride (9CI) (CA INDEX NAME)

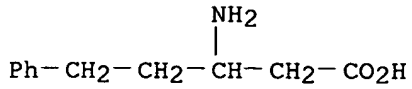


● HCl

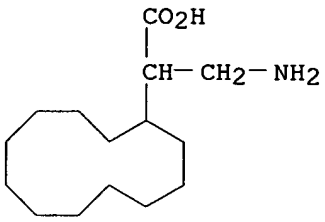
IT **91247-38-0P 213192-16-6P 213192-17-7P 213192-18-8P 213192-19-9P 213192-49-5P 213192-68-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-**epileptogenic** agents)

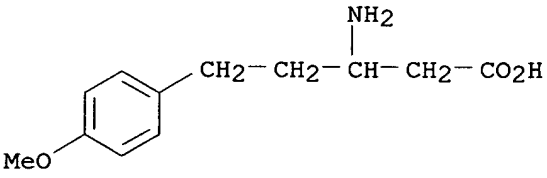
RN 91247-38-0 CAPLUS
CN Benzenepentanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



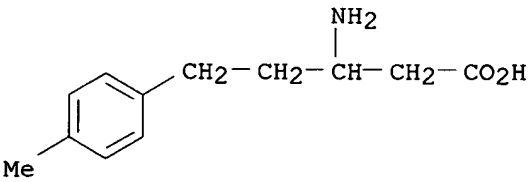
RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)



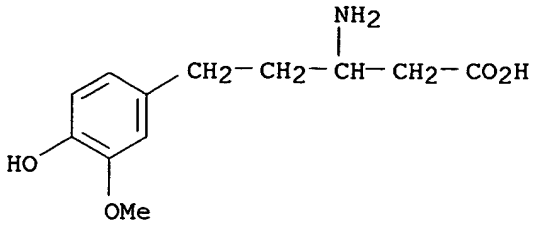
RN 213192-17-7 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-methoxy- (9CI) (CA INDEX NAME)



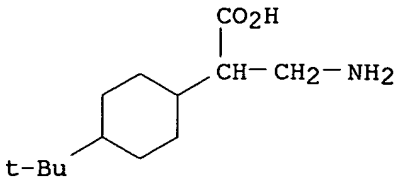
RN 213192-18-8 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-methyl- (9CI) (CA INDEX NAME)



RN 213192-19-9 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)

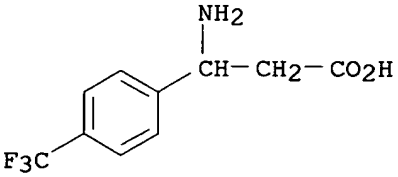


RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



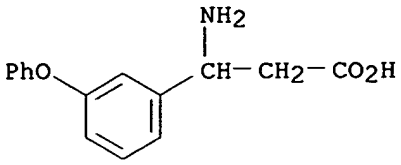
● HCl

RN 213192-68-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

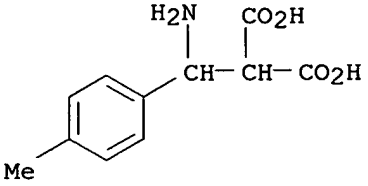


● HCl

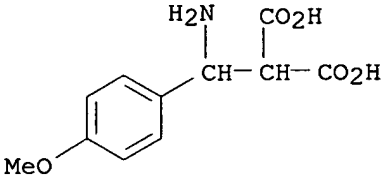
IT **202131-32-6 460039-79-6 460039-80-9 460039-81-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**epileptogenic** agents)
RN 202131-32-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy- (9CI) (CA INDEX NAME)



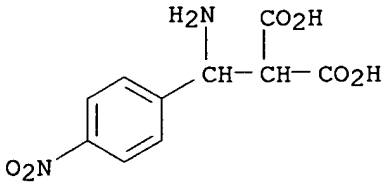
RN 460039-79-6 CAPLUS
CN Propanedioic acid, [amino(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



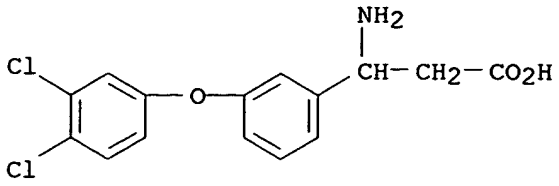
RN 460039-80-9 CAPLUS
CN Propanedioic acid, [amino(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 460039-81-0 CAPLUS
CN Propanedioic acid, [amino(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)

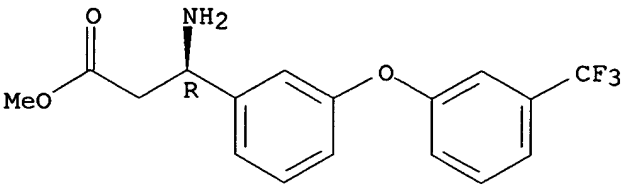


IT **213192-53-1P 460039-72-9P 460039-73-0P**
460039-74-1P 460039-75-2P 460039-76-3P
460039-77-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(anti-**epileptogenic** agents)
RN 213192-53-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)- (9CI) (CA INDEX NAME)



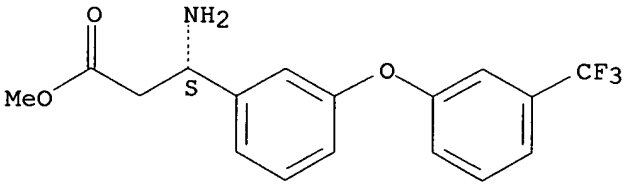
RN 460039-72-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



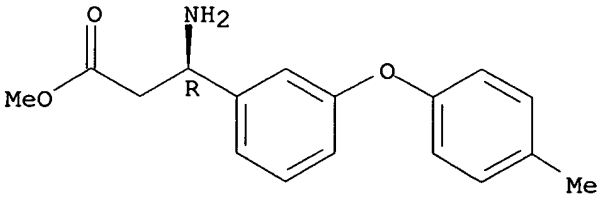
RN 460039-73-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]-, methyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



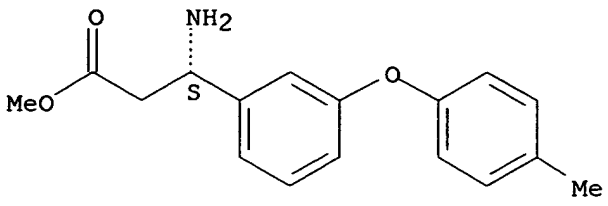
RN 460039-74-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



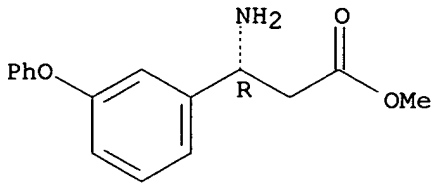
RN 460039-75-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)-, methyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



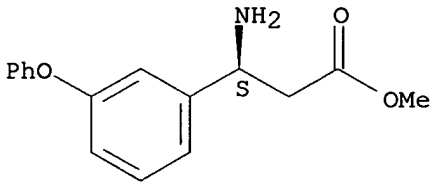
RN 460039-76-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

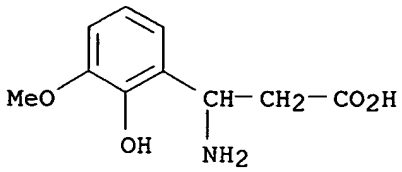


RN 460039-77-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-phenoxy-, methyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

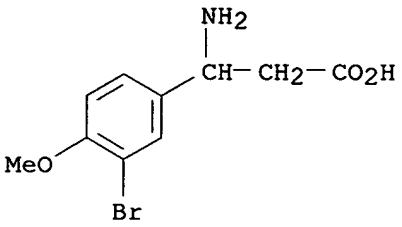
Absolute stereochemistry.



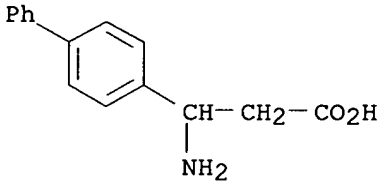
IT **32906-18-6P 34840-91-0P 63974-15-2P**
68208-20-8P 138621-64-4P 193633-48-6P
213192-55-3P 213192-56-4P 213192-57-5P
213192-61-1P 213192-63-3P 213192-64-4P
213192-65-5P 213192-67-7P 213192-76-8P
460039-51-4P 460039-64-9P 460039-65-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(anti-**epileptogenic** agents)
RN 32906-18-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



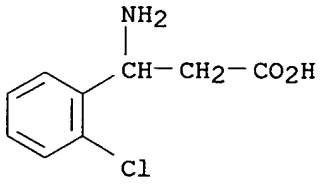
RN 34840-91-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-bromo-4-methoxy- (9CI) (CA INDEX NAME)



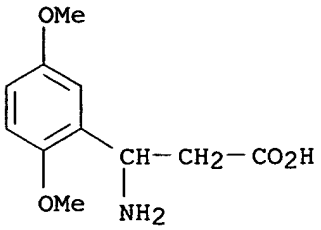
RN 63974-15-2 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



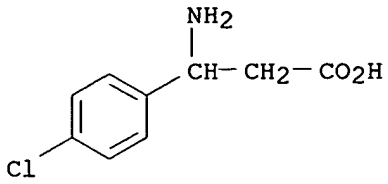
RN 68208-20-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-chloro- (9CI) (CA INDEX NAME)



RN 138621-64-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2,5-dimethoxy- (9CI) (CA INDEX NAME)

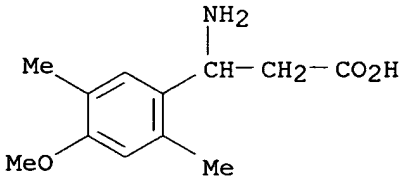


RN 193633-48-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-chloro-, hydrochloride (9CI) (CA INDEX NAME)

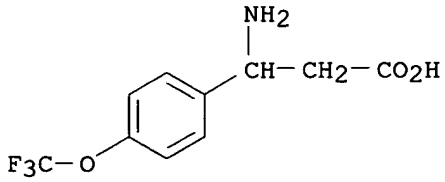


● HCl

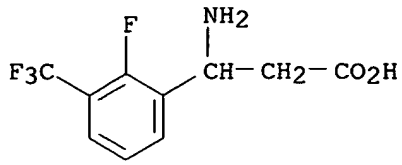
RN 213192-55-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methoxy-2,5-dimethyl- (9CI) (CA INDEX NAME)



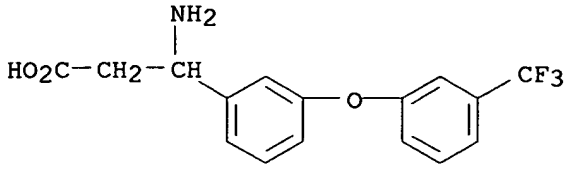
RN 213192-56-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



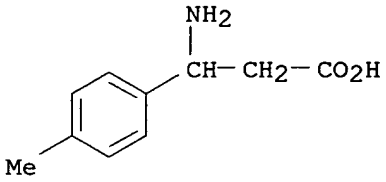
RN 213192-57-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-fluoro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 213192-61-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]- (9CI) (CA INDEX NAME)

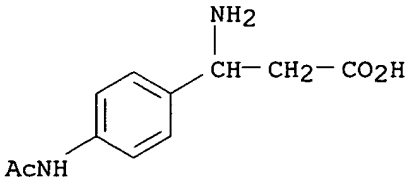


RN 213192-63-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

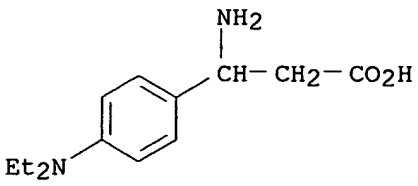
RN 213192-64-4 CAPLUS
CN Benzenepropanoic acid, 4-(acetylamino)-.beta.-amino-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

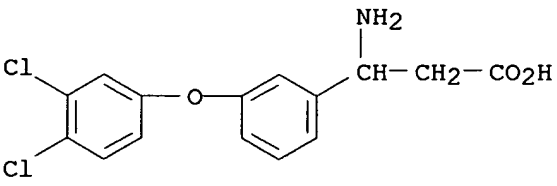
RN 213192-65-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(diethylamino)-, monohydrochloride

(9CI) (CA INDEX NAME)



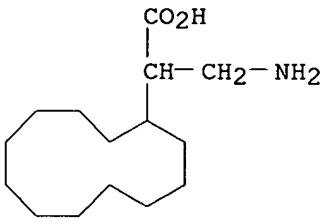
● HCl

RN 213192-67-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)-, hydrochloride (9CI) (CA INDEX NAME)



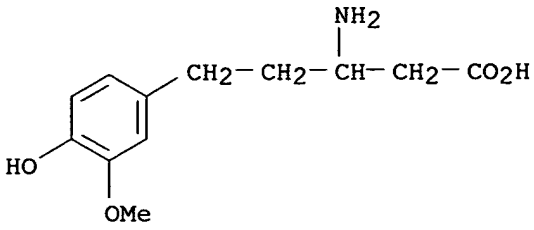
● HCl

RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

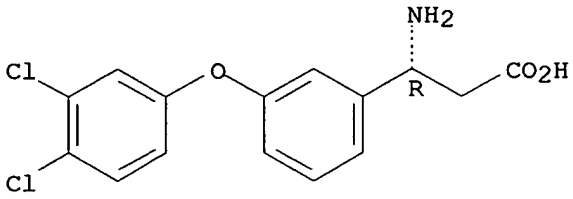
RN 460039-51-4 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-hydroxy-3-methoxy-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 460039-64-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)-, hydrochloride, (.beta.R)- (9CI) (CA INDEX NAME)

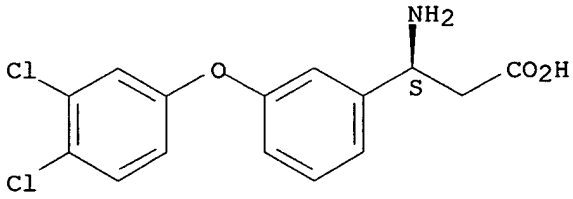
Absolute stereochemistry.



● HCl

RN 460039-65-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)-, hydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1998:621100 CAPLUS
DN 129:239901
TI Anti-**epileptogenic** agents, and preparation thereof
IN Weaver, Donald F.; Milne, Paul H.; Tan, Christopher Y. K.; Carran, John R.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English

Applicant's PCT.

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840055	A2	19980917	WO 1998-CA244	19980312
	WO 9840055	A3	19990218		
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	AU 9864923	A1	19980929	AU 1998-64923	19980312
	EP 969823	A2	20000112	EP 1998-910555	19980312
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	US 2002025949	A1	20020228	US 2001-932676	20010816
PRAI	US 1997-41140P	P	19970312		
	US 1998-73536P	P	19980203		
	US 1998-41371	A3	19980311		
	WO 1998-CA244	W	19980312		

OS MARPAT 129:239901
AB Methods and compds. useful for the inhibition of convulsive disorders, including epilepsy, are disclosed. The methods and compds. of the invention inhibit or prevent ictogenesis and **epileptogenesis**. Methods for prepg. the compds. of the invention are also described.
IT **19947-39-8P 32906-18-6P 34840-91-0P**
54503-17-2P 63974-15-2P 68208-16-2P
68208-17-3P 68208-18-4P 68208-20-8P
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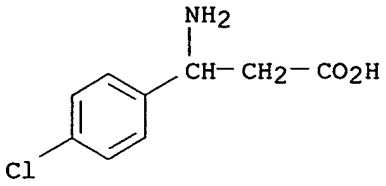
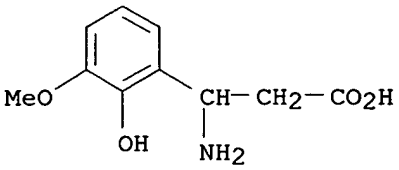
213192-57-5P 213192-58-6P 213192-59-7P
213192-60-0P 213192-61-1P 213192-62-2P
213192-63-3P 213192-64-4P 213192-65-5P
213192-66-6P 213192-67-7P 213192-68-8P
213192-76-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-**epileptogenic** agents for convulsive disorder treatment, and prepn. thereof)

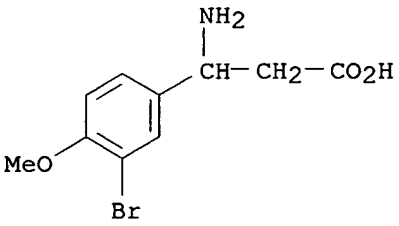
RN 19947-39-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-chloro- (9CI) (CA INDEX NAME)



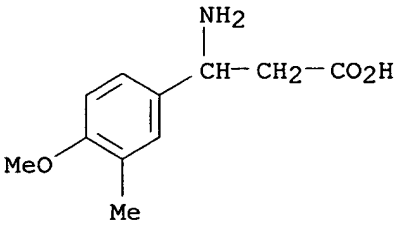
RN 32906-18-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



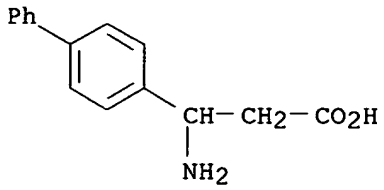
RN 34840-91-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-bromo-4-methoxy- (9CI) (CA INDEX NAME)



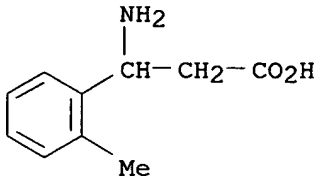
RN 54503-17-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methoxy-3-methyl- (9CI) (CA INDEX NAME)



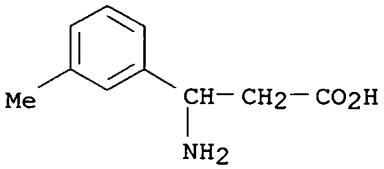
RN 63974-15-2 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



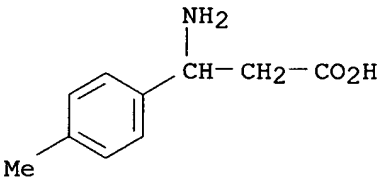
RN 68208-16-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-methyl- (9CI) (CA INDEX NAME)



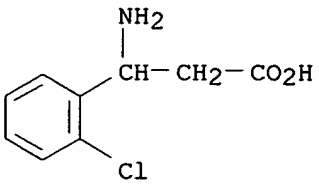
RN 68208-17-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-methyl- (9CI) (CA INDEX NAME)



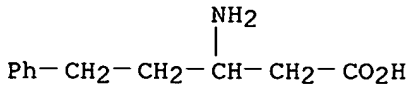
RN 68208-18-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methyl- (9CI) (CA INDEX NAME)



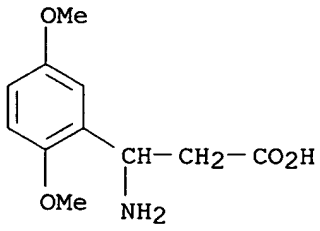
RN 68208-20-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-chloro- (9CI) (CA INDEX NAME)



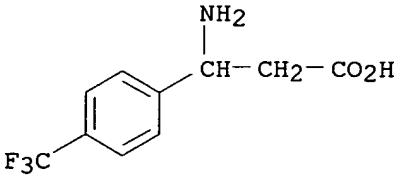
RN 91247-38-0 CAPLUS
CN Benzenepentanoic acid, .beta.-amino- (9CI) (CA INDEX NAME)



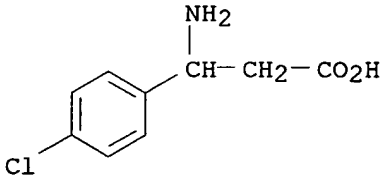
RN 138621-64-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2,5-dimethoxy- (9CI) (CA INDEX NAME)



RN 180263-44-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)

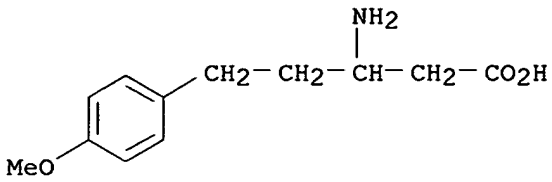


RN 193633-48-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-chloro-, hydrochloride (9CI) (CA INDEX NAME)

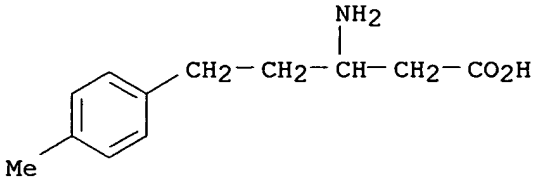


● HCl

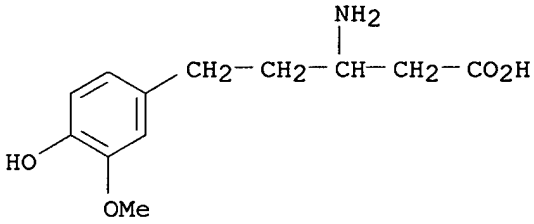
RN 213192-17-7 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-methoxy- (9CI) (CA INDEX NAME)



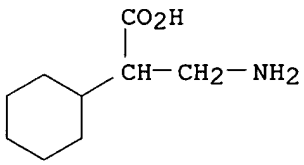
RN 213192-18-8 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-methyl- (9CI) (CA INDEX NAME)



RN 213192-19-9 CAPLUS
CN Benzenepentanoic acid, .beta.-amino-4-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)

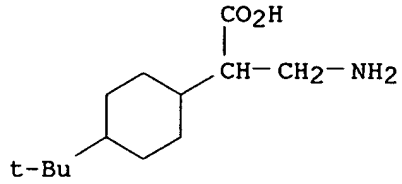


RN 213192-48-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



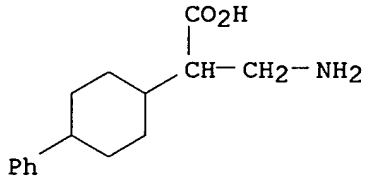
● HCl

RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



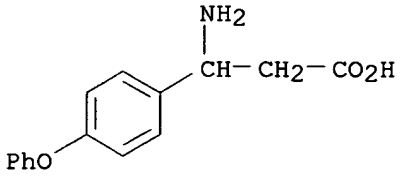
● HCl

RN 213192-50-8 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

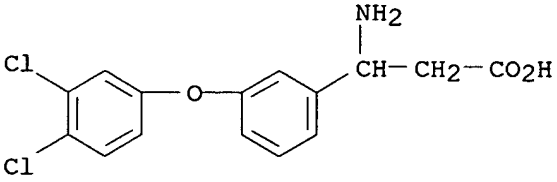


● HCl

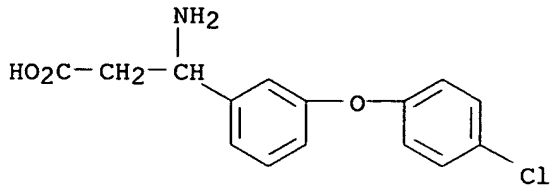
RN 213192-51-9 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-phenoxy- (9CI) (CA INDEX NAME)



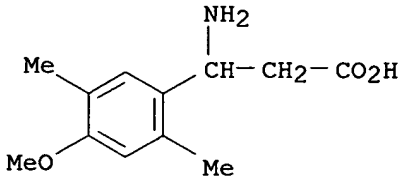
RN 213192-53-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)- (9CI) (CA INDEX NAME)



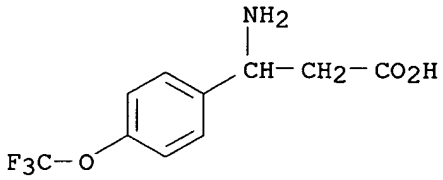
RN 213192-54-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-chlorophenoxy)- (9CI) (CA INDEX NAME)



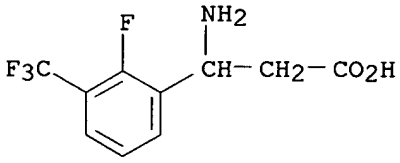
RN 213192-55-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methoxy-2,5-dimethyl- (9CI) (CA INDEX NAME)



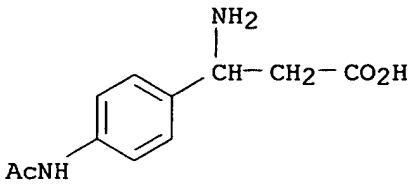
RN 213192-56-4 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



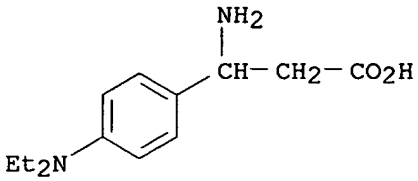
RN 213192-57-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-2-fluoro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



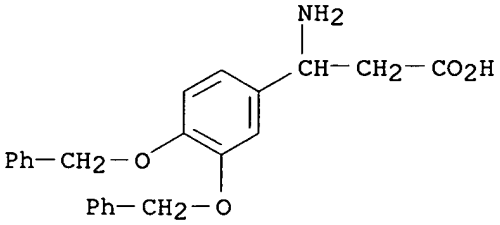
RN 213192-58-6 CAPLUS
CN Benzenepropanoic acid, 4-(acetylamino)-.beta.-amino- (9CI) (CA INDEX NAME)



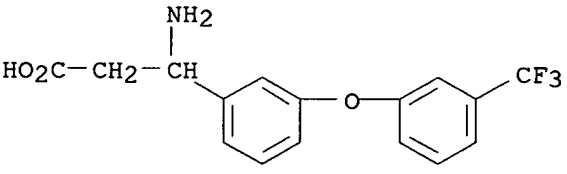
RN 213192-59-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(diethylamino)- (9CI) (CA INDEX NAME)



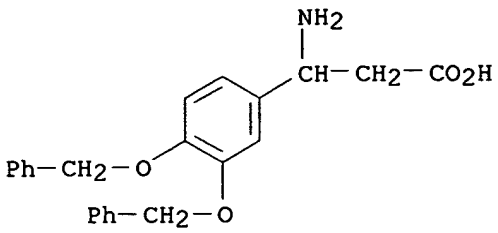
RN 213192-60-0 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3,4-bis(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 213192-61-1 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-[3-(trifluoromethyl)phenoxy]- (9CI) (CA INDEX NAME)

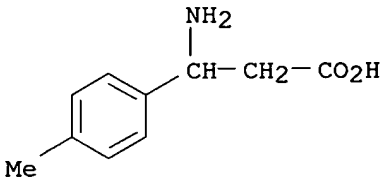


RN 213192-62-2 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3,4-bis(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)



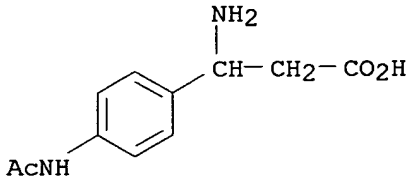
● HCl

RN 213192-63-3 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-methyl-, hydrochloride (9CI) (CA INDEX NAME)



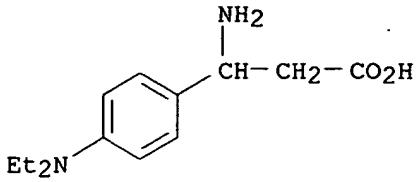
● HCl

RN 213192-64-4 CAPLUS
CN Benzenepropanoic acid, 4-(acetylamino)-.beta.-amino-, monohydrochloride (9CI) (CA INDEX NAME)



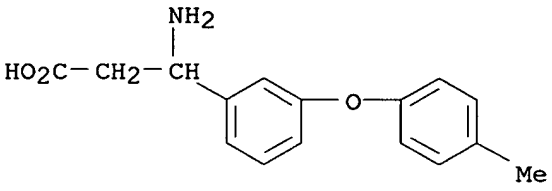
● HCl

RN 213192-65-5 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(diethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)

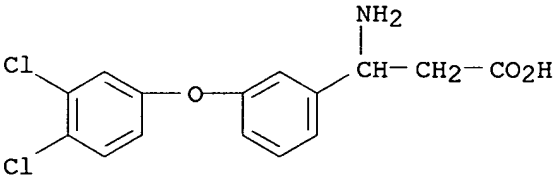


● HCl

RN 213192-66-6 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(4-methylphenoxy)- (9CI) (CA INDEX NAME)

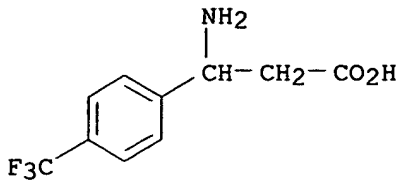


RN 213192-67-7 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-3-(3,4-dichlorophenoxy)-, hydrochloride (9CI) (CA INDEX NAME)



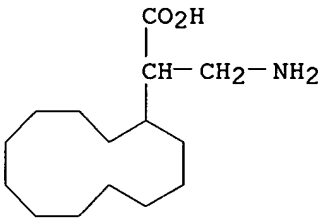
● HCl

RN 213192-68-8 CAPLUS
CN Benzenepropanoic acid, .beta.-amino-4-(trifluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



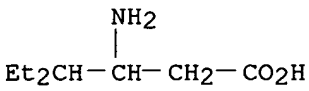
● HCl

RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

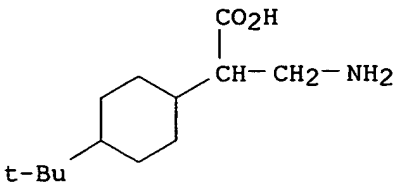


● HCl

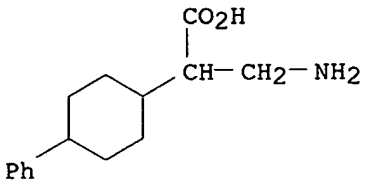
IT **204191-42-4 213192-14-4 213192-15-5**
213192-16-6 213192-20-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**epileptogenic** agents for convulsive disorder treatment, and prepn. thereof)
RN 204191-42-4 CAPLUS
CN Hexanoic acid, 3-amino-4-ethyl- (9CI) (CA INDEX NAME)



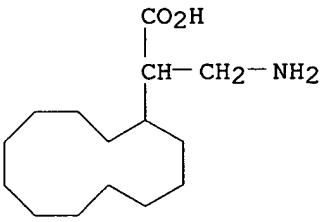
RN 213192-14-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



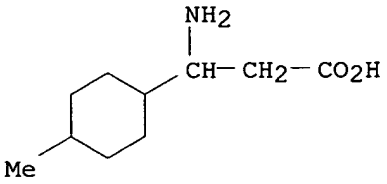
RN 213192-15-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl- (9CI) (CA INDEX NAME)



RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)



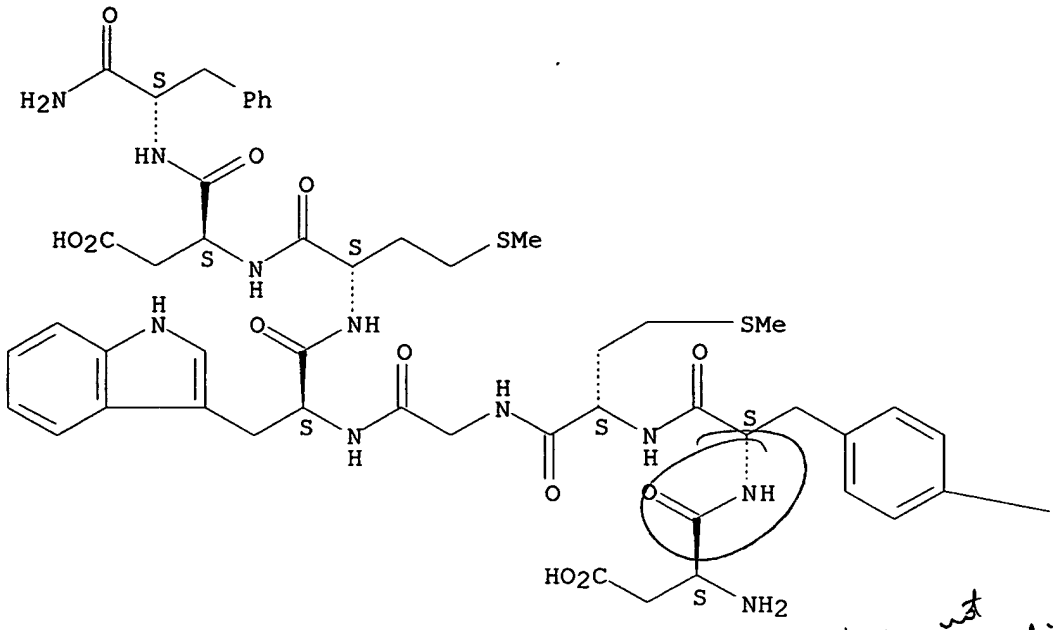
RN 213192-20-2 CAPLUS
CN Cyclohexanepropanoic acid, .beta.-amino-4-methyl- (9CI) (CA INDEX NAME)



L21 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1996:542463 CAPLUS
DN 125:192109
TI Neuropeptides-immunoreactivity and their mRNA expression in kindling: functional implications for limbic **epileptogenesis**
AU Schwarzer, Christoph; Sperk, Gunther; Samanin, Rosario; Rizzi, Massimo; Gariboldi, Marco; Vezzani, Annamaria
CS Istituto di Ricerche Farmacologiche Mario Negri, Milan, 20157, Italy
SO Brain Research Reviews (1996), 22(1), 27-50
CODEN: BRERD2; ISSN: 0165-0173
PB Elsevier
DT Journal; General Review
LA English
AB A review, with 120 refs., of the information on the pathol. changes and functional modifications in neuropeptide systems of the hippocampal formation in kindling and other models of limbic epilepsy. This is particularly true in the hippocampus where the expression of various neuropeptides has been reported to change in distinct neuronal populations in response to seizure activity. This will be done by presenting a study in which we investigate the changes in the expression of somatostatin, neuropeptide Y (NPY), neurokinin B (NKB) and cholecystokinin-octapeptide (CCK) in the rat hippocampal principal neurons during and after kindling of the hippocampus using immunocytochem. and in situ hybridization anal. of mRNA. NPY-IR was transiently expressed in the granule cells/mossy fibers after the preconvulsive stage 2 and 2 days but not 1 wk after three consecutive tonic-clonic seizures (stage 5). A more pronounced increase was obsd. in NKB-IR lasting for 1 wk after kindling acquisition. Only the NKB mRNA expression was enhanced in granule cells at these intervals. At stages 2 and 5, somatostatin- and NPY-IR and their mRNA levels were markedly increased in interneurons in the deep hilus and in the polymorphic cell layer and their presumed projections to the outer mol. layer of the dentate gyrus. NKB- and CCK-IR and their mRNAs were highly expressed in basket cells at both stages of kindling. Their IR was increased in the inner mol. layer of the dentate gyrus in the ventral hippocampus. Peptide-contg. neurons in the hilus appeared well preserved in spite of a redn. of Nissl stained cells by 24% in the stimulated and contralateral hippocampus at stage 5. In the hippocampus proper, somatostatin and NPY-IR were enhanced in the stratum lacunosum moleculare while CCK-IR fibers and its mRNA were particularly expressed in the pyramidal cell layer. The no. of somatostatin-, NKB- and CCK-IR cells was increased in the subiculum. The intensity of these changes was similar 2 days after stages 2 or 5 of kindling. Less pronounced effects were obsd. 1 wk after kindling completion. These results, in the frame of the literature data, suggest that lasting functional changes occur in distinct neuropeptide-contg. neurons during limbic **epileptogenesis**. This may have profound effects on synaptic transmission and contribute to modulate hippocampal excitability.
IT **25126-32-3**, Cholecystokinin-8 (pig)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(neuropeptides and their mRNA expression in kindling in relation to limbic **epileptogenesis**)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



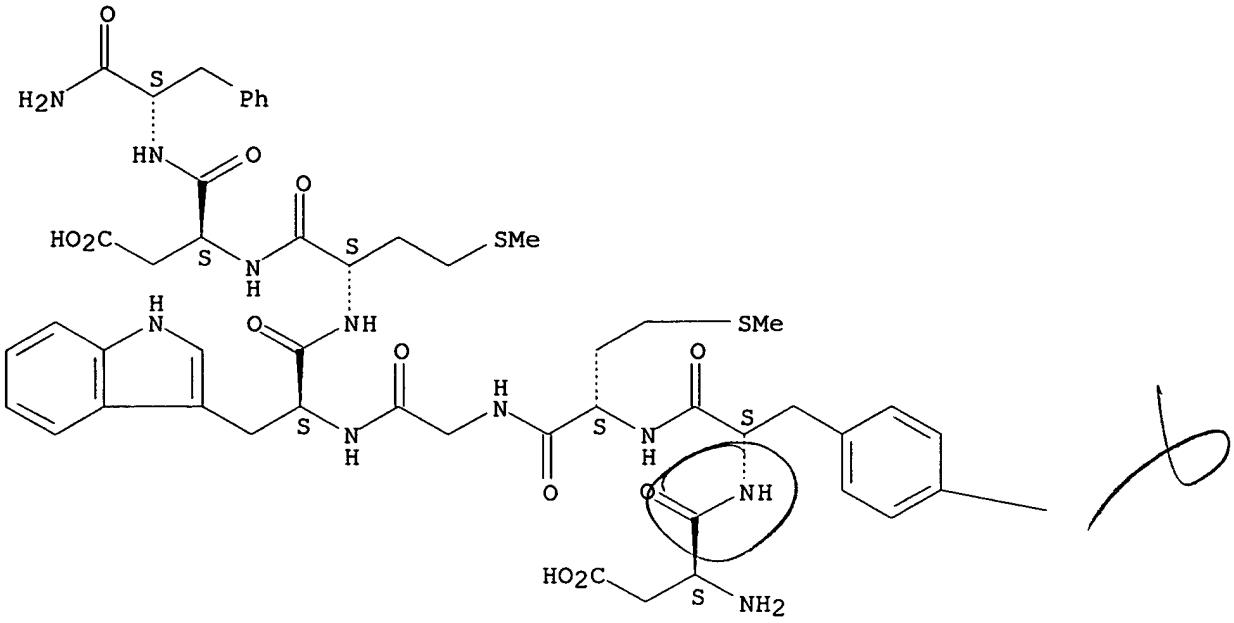
PAGE 1-B

—OSO_3H

L21 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1995:367018 CAPLUS
DN 122:123633
TI Cholecystokinin potentiates morphine anticonvulsant action through both CCK-A and CCK-B receptors
AU Legido, A.; Adler, M. W.; Karkanias, C.; Geller, E. B.; Bradley, E.; Greenstein, J. I.; Grover, W. D.
CS Temple University School of Medicine, Philadelphia, PA, USA
SO Neuropeptides (Edinburgh) (1995), 28(2), 107-13
CODEN: NRPPDD; ISSN: 0143-4179
PB Churchill Livingstone
DT Journal
LA English
AB Recent studies have suggested that cholecystokinin may have a role in modulating the effects of the endogenous opioid system in physiol. functions such as thermoregulation and pain control. However, the possible interaction of cholecystokinin and morphine in **epileptogenesis** is unknown. The authors studied the effect of s.c. morphine and intracerebroventricularly administered cholecystokinin octapeptide sulfate ester and receptor antagonists CCK-A (MK 329) and CCK-B (L 365,260) on seizures provoked by maximal electroshock in male Sprague-Dawley rats. Seizures were induced through electrode-gel-coated ear clip electrodes by a high voltage, high internal resistance const. current generator, 30 min after morphine administration and 10 min after cholecystokinin-8-SE, CCK-A and CCK-B infusion. Morphine decreased the length of the tonic component of the seizure and cholecystokinin potentiated this decrease. Cholecystokinin antagonists blocked the effects of both cholecystokinin and morphine. The results suggest that cholecystokinin acts as an endogenous agonist with opioids in the regulation of seizures susceptibility through both CCK-A and B receptors and may be responsible for part of the anticonvulsant action of morphine.
IT **25126-32-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholecystokinin potentiates morphine anticonvulsant action through both CCK-A and CCK-B receptors)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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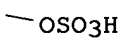
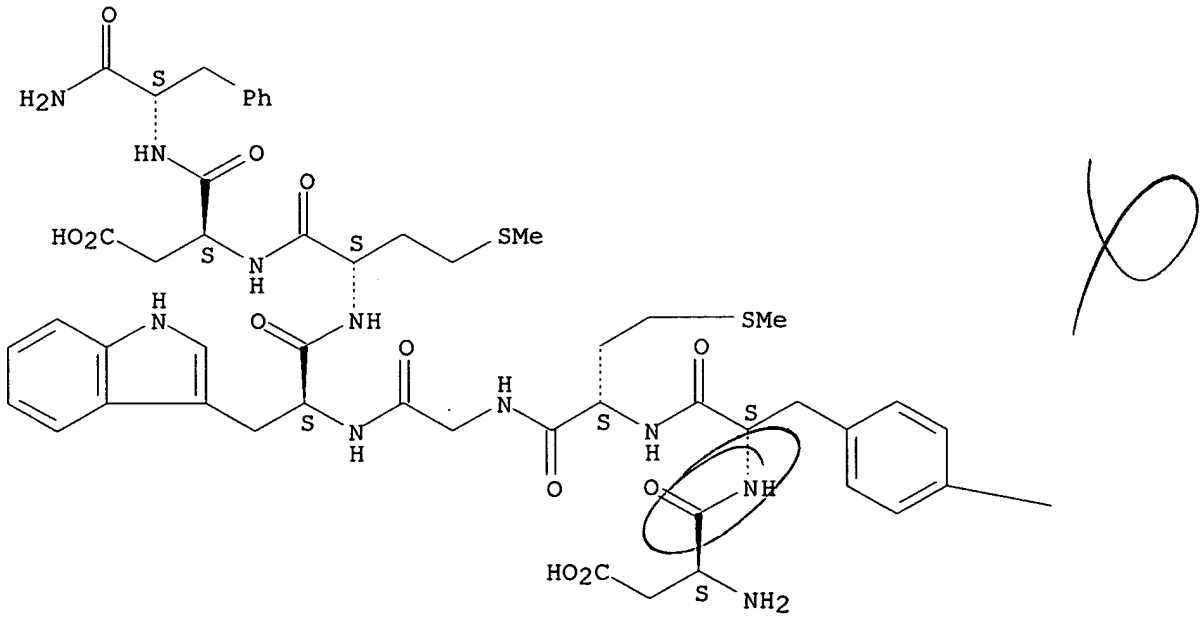
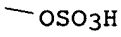


L21 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1994:70037 CAPLUS
DN 120:70037
TI Effect of ceruletide on **epileptogenesis** in amygdaloid kindled rats
AU Yamamoto, Yoshitaka; Itano, Toshifumi; Miyamoto, Osamu; Tokuda, Masaaki; Matsui, Hideki; Janjua, Najma A.; Suwaki, Hiroshi; Okada, Yasushi; Negi, Tetsuro; et al.
CS Physiology, Kagawa, 761-07, Japan
SO Brain Research (1993), 630(1-2), 353-6
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB The inhibitory effects of ceruletide (CLT), a CCK-8-like peptide, were investigated in the **epileptogenesis** in the amygdaloid kindled rats. Lower doses of CLT (20-80 .mu.g/kg) inhibited the progression of kindling process. After acquiring C5 stage, a higher dose (160 .mu.g/kg) was required to suppress the seizure susceptibility. These results, in light of several previous studies showing no serious side effects, suggest that CLT might be useful as an anti-**epileptogenic** agent for clin. usage.
IT **25126-32-3D**, CCK-8, deriv.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

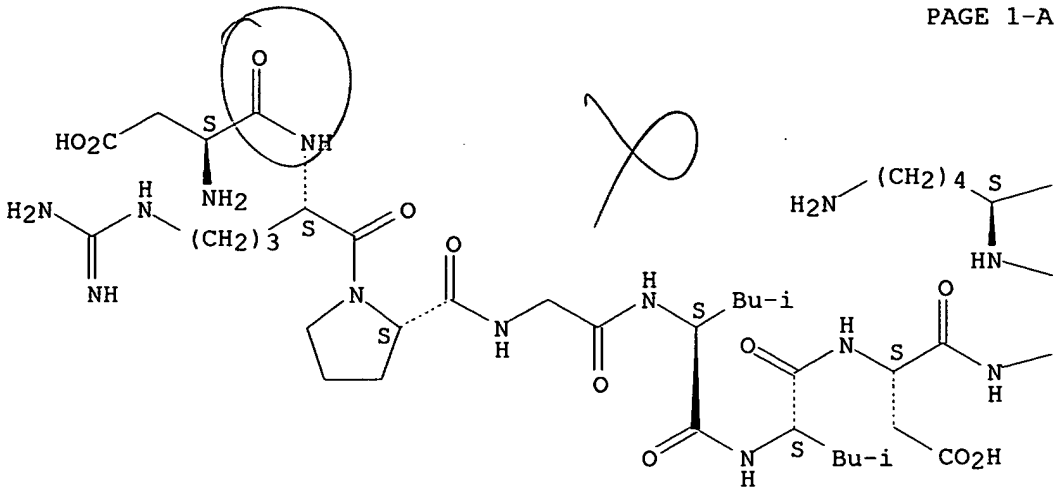




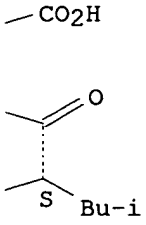
L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1992:445867 CAPLUS
DN 117:45867
TI **Epileptogenic** activity of two peptides derived from diazepam-binding inhibitor after intrahippocampal injection in rats
AU Vezzani, A.; Serafini, R.; Stasi, M. A.; Samanin, R.; Ferrarese, C.
CS Ist. Ric. Farmacol. "Mario Negri", Milan, 20157, Italy
SO Epilepsia (1991), 32(5), 597-603
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB Peptides DBI 42-50 (DRPGLLDLK) and DBI 43-50 (RPGLLDLK) are synthetic fragments of an 18-amino acid peptide called octadecaneuropeptide (QATVGDVNTDRPGLLDLK), a brain deriv. of diazepam-binding inhibitor (DBI). The two peptides were unilaterally injected into the dorsal hippocampus (granule cells of dentate gyrus) of freely moving adult rats. The EEG pattern was continuously recorded from bilateral hippocampal and cortical electrodes, and the animals' behavior was obsd. throughout the expt. A dose of 100 nmol peptide 42-50 was required to cause reliably EEG alterations (seizures and spiking). EEG changes, defined as seizures, were characterized by discrete repetitive periods of high-frequency and(or) multispike complexes and(or) high-voltage synchronized spike or wave activity. EEG seizures were often assocd. with a frozen appearance of the animal and wet dog shakes. Tonic-clonic convulsions were not obsd. EEG seizures induced by peptide 42-50 were prevented by 90 mg/kg PK 11195, a selective antagonist of a novel GABAA receptor-linked subtype of a benzodiazepine (BDZ) receptor, but were unaffected by flumazenil, an agonist of the central type of BDZ receptor and by D(-)2-amino-7-phosphonoheptanoic acid, a selective antagonist of the N-methyl-D-aspartate subtype of excitatory amino acid receptors. Light microscopy showed no neuropathol. changes in the injected hippocampus. Thus, these DBI-derived peptide fragments induce a typical pattern of limbic seizures in rats. DBI and(or) its natural processing products may play a role in the pathophysiol. of epilepsy.
IT **120550-29-0**
RL: BIOL (Biological study)
(brain elec. activity changes and seizure activity induced by, epilepsy pathogenesis in relation to)
RN 120550-29-0 CAPLUS
CN L-Lysine, N2-[N-[N-[N-[N-[N-[1-(N2-L-.alpha.-aspartyl-L-arginyl)-L-prolyl]glycyl]-L-leucyl]-L-leucyl]-L-.alpha.-aspartyl]-L-leucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

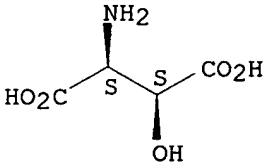


PAGE 1-B



L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1988:421149 CAPLUS
DN 109:21149
TI On the **epileptogenic** effects of kainic acid and dihydrokainic acid in the dentate gyrus of the rat
AU Butcher, S. P.; Jacobson, I.; Hamberger, A.
CS Inst. Neurobiol., Univ. Goteborg, Goteborg, Swed.
SO Neuropharmacology (1988), 27(4), 375-81
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB The in vivo effects of the acidic amino acid receptor agonist kainic acid and of the inhibitors of glutamate uptake dihydrokainic acid and threo-3-hydroxyaspartate on spontaneous activity and perforant path evoked field potentials were examd. in the dentate gyrus of the rat. The effect of these compds. on extracellular levels of endogenous amino acids in the hippocampus was assessed simultaneously using in vivo microdialysis. Kainic acid (10-100 .mu.M) and dihydrokainic acid (1-10 mM) both evoked epileptiform activity and an apparent loss of recurrent inhibition (as assessed using the paired-pulse technique). Extracellular increases in taurine, alanine, and phosphoethanolamine were noted following administration of kainate (100 .mu.M) and dihydrokainate (1-10 mM). An increase in extracellular glutamate and aspartate was also noted in rats treated with dihydrokainate (100 .mu.M-10 mM). In contrast, threo-3-hydroxyaspartate did not induce epileptiform activity, suggesting that the **epileptogenic** effects of dihydrokainate and kainate are not mediated by inhibition of uptake. The effect of the N-methyl-D-aspartate receptor antagonist D-2-amino-5-phosphonovalerate on these responses was studied. This compd. attenuated the epileptiform activity and reversed the apparent loss of recurrent inhibition in response to both kainic acid and dihydrokainic acid. These data suggest that activation of N-methyl-D-aspartate receptors underlies the **epileptogenic** effects of both compds., and the possible mechanisms which might be involved in this response are discussed.
IT **7298-99-9**
RL: BIOL (Biological study)
(**epileptogenic** activity of, amino acid receptors and uptake in)
RN 7298-99-9 CAPLUS
CN L-Aspartic acid, 3-hydroxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L5             SCREEN 2026 OR  2039 OR  2045 OR  2046 OR  2047
L6             STRUCTURE UPLOADED
L7             QUE L6 NOT L5
L8          24 S L7 SSS SAM
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L16            QUE L15 AND L13 NOT L14
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L18      29852 S L16 SSS FUL

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L21          8 S L19 AND L20
L22      10468 S ANTIEPILEPT?
L23         34 S L18 AND L22

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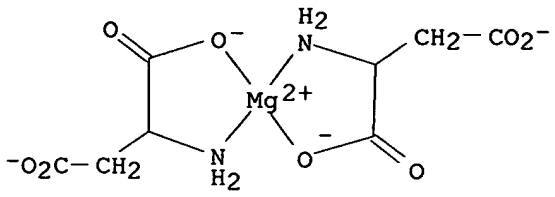
L24 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 2002:381826 CAPLUS
DN 136:350580
TI Method for treating glioma aggravated with epileptic syndrome
IN Korytova, L. I.; Zhabina, R. M.; Sokurenko, V. P.; Vartanyan, L. P.
PA Tsentral'nyi Nauchno-Issledovatel'skii Rentgenoradiologicheskii Institut, Russia
SO Russ., No pp. given
CODEN: RUXXE7
DT Patent
LA Russian
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI RU 2166948	C1	20010520	RU 2000-113130	20000529
PRAI RU 2000-113130		20000529		

AB The proposed method involves per os administration of riboxin to a patient, after surgical removal of the tumor, at a dose of 0.2 g, 3 times a day, for 5-10 days. Radiation therapy is started at the same time. I.v. (and later peroral) riboxin and proxiphein are administered. Riboxin is i.v. injected at a dose of 10 mL during the first two weeks and then per os at a dose of 0.2 g three times a day for up to 3 mo. Proxiphein is administered according to the following scheme: 2 days the dose is 0.25 g once a day, two days - 0.25 g twice a day, and then, the dose is 0.25 g three times a day during 40-45 days. The chemotherapy course is repeated 4-5 wk later. Benzonal is applied as an anticonvulsive prepn. at a dose of 0.1 g or finlepsin at a dose of 0.2 g 3 times a day during the first two weeks and then two times a day to the end of the chemotherapy course and later at a dose of 1 tablet before going to bed for not less than 2-3 yr. Enhanced effectiveness of the treatment was achieved by the proposed method.
IT **8076-65-1**, Panangin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of glioma aggravated with epileptic syndrome)
RN 8076-65-1 CAPLUS
CN Aspartic acid, monopotassium salt, mixt. with potassium hydrogen (T-4)-bis[aspartato(2-)-.kappa.N,.kappa.O1]magnesate(2-) (9CI) (CA INDEX NAME)

CM 1

CRN 32679-51-9
CMF C8 H10 Mg N2 O8 . H . K
CCI CCS

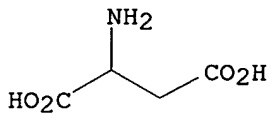


● H^+

● K^+

CM 2

CRN 923-09-1
CMF C4 H7 N O4 . K



● K

L24 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 2000:824407 CAPLUS
DN 134:14025
TI Structure and alternative splicing of human brain T calcium channel .alpha.-subunit genes
IN Mittman, Scott; Agnew, William S.
PA The Johns Hopkins University, USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000070044	A2	20001123	WO 2000-US12383	20000508
WO 2000070044	A3	20010517		

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-134063P P 19990513
US 1999-137547P P 19990604

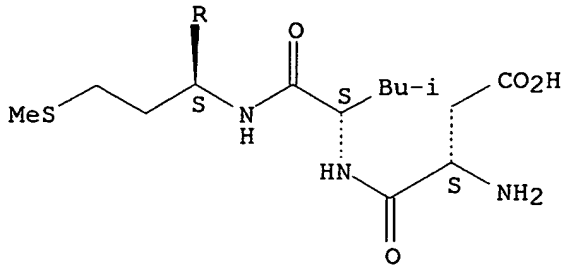
AB The structures of CACNA1G and CACNA1I , the genes encoding the human brain T Ca2+ channel .alpha.1G and .alpha.1I subunits, resp., were detd. by comparison of PCR-amplified brain cDNA and genomic sequences. CACNA1G consists of at least 38 exons spanning at least 66,490 bp of chromosome 17q22. Alternative splicing of the RNA occurs at six sites: cassette exons 14, 26, 34 and 35, an internal donor in exon 25 and protein-coding intron 38B. Addnl., the RNA can be polyadenylated at either of 2 sites. Alternative splicing of CANCA1G RNA may lead to expression of as many as 64 distinct protein products, ranging from 2171 to 2377 amino acid residues, with as many as 45 potential phosphorylation sites. CACNA1I consists of at least 37 exons spanning at least 116,390 bp of chromosome 22q12.3-13.2. Alternative splicing of the gene occurs at 3 sites: cassette exon 9, an alternative acceptor in exon 33 and mutually exclusive 3' exons 36B and 37. Alternative splicing of CANCA1I RNA may lead to expression of as many as 8 distinct protein products, ranging from 1968 to 2223 amino acid residues, with as many as 28 potential phosphorylation sites. Mol. diversity generated by alternative splicing and post-translation modification of these and other members of the T .alpha.1 subunit gene family may account for the obsd. heterogeneity of T currents in central neurons. The invention also provides screening methods for **antiepileptic** drugs.

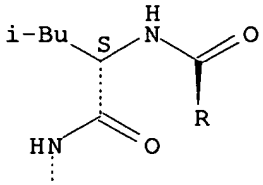
IT **308369-85-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; structure and alternative splicing of human brain T calcium channel .alpha.-subunit genes)

RN 308369-85-9 CAPLUS
CN L-Serine, L-.alpha.-aspartyl-L-leucyl-L-methionyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-valyl-L-isoleucyl-L-alanyl-L-serylglycyl-L-seryl-L-seryl-L-alanyl-L-seryl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

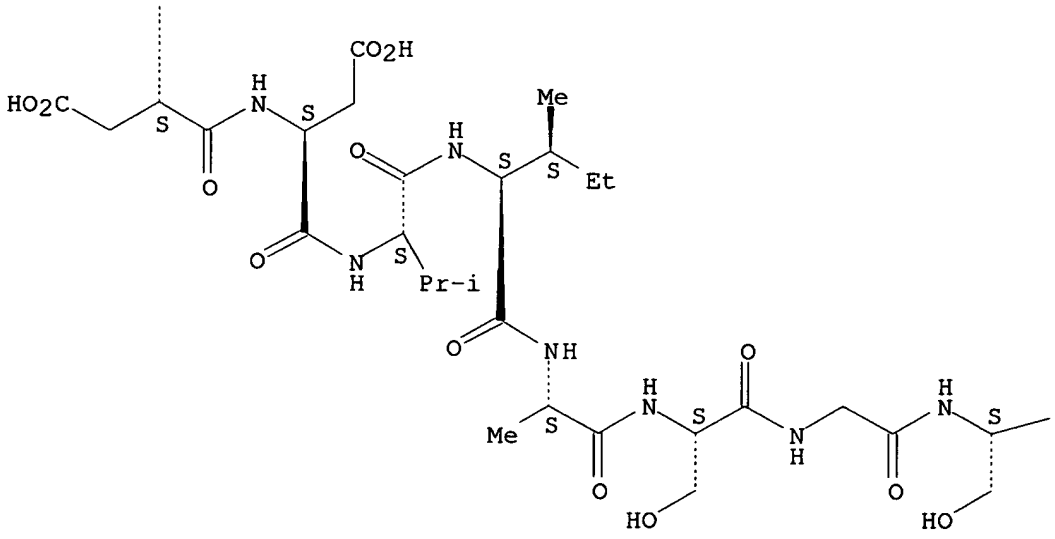
Absolute stereochemistry.

PAGE 1-A

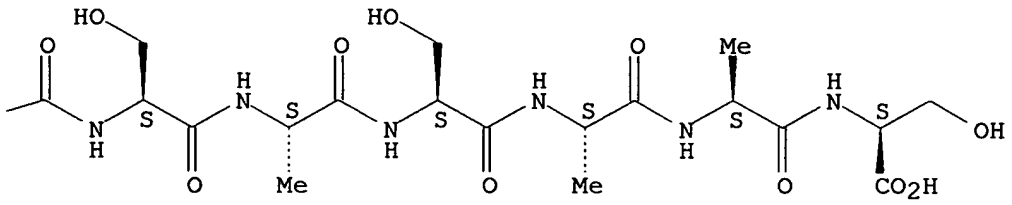




PAGE 2-A

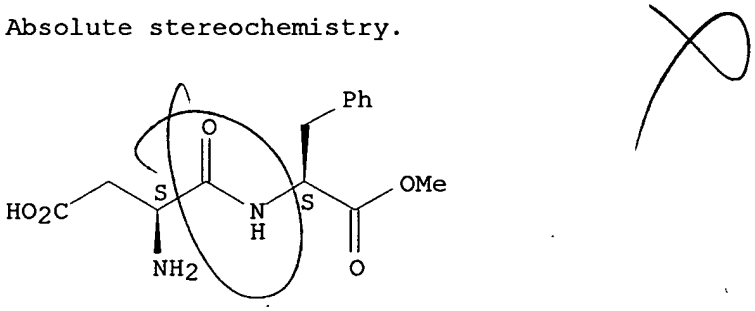


PAGE 2-B



L24 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1996:749893 CAPLUS
DN 126:26397
TI The effect of aspartame on seizure susceptibility and the anticonvulsant action of ethosuximide, valproate and phenytoin in mice
AU Helali, N. Y.; El-Kashef, H.; Salem, H.; Gamiel, N.; Elmazar, M. M. A.
CS Faculty Pharmacy, Mansoura University, Egypt
SO Saudi Pharmaceutical Journal (1996), 4(3-4), 149-156
CODEN: SPJOEM; ISSN: 1319-0164
PB Saudi Pharmaceutical Society
DT Journal
LA English
AB Aspartame (APM) when given as a single (1 g/kg, orally) or repeated (100 mg/kg, orally for 14 days) neither affected the spontaneous locomotor activity of mice in an open field, nor altered pentylenetetrazol (PTZ)-induced seizure threshold. Subacute, but not acute, APM administration was found to decrease the anticonvulsant activity of ethosuximide (ETH) and valproate (VPA) in PTZ-induced seizure threshold, and of phenytoin (PHT) in PTZ-induced generalized tonic clonic seizures. The antagonism of the anticonvulsant activity of ETH, VPA and PHT was not due to alterations of plasma levels or pharmacokinetics of the **antiepileptic** drugs, but could be due to an increase of brain excitatory and/or decrease of brain inhibitory neurotransmitters. Subacute APM administration was found to decrease brain adrenaline and noradrenaline levels which might increase seizure susceptibility in mice. VPA and PHT, but not ETH, were found to antagonize subacute APM-induced decrease in brain adrenaline level. On the other hand, subacute APM administration was found to partially antagonize VPA induced decrease in brain aspartate and increase in GABA levels; and PHT-induced decrease in brain glutamate and increase in GABA levels.
IT **22839-47-0**, Aspartame
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effect of aspartame on seizure susceptibility and on anticonvulsant action of ethosuximide, valproate and phenytoin)
RN 22839-47-0 CAPLUS
CN L-Phenylalanine, L-.alpha.-aspartyl-, 2-methyl ester (9CI) (CA INDEX NAME)

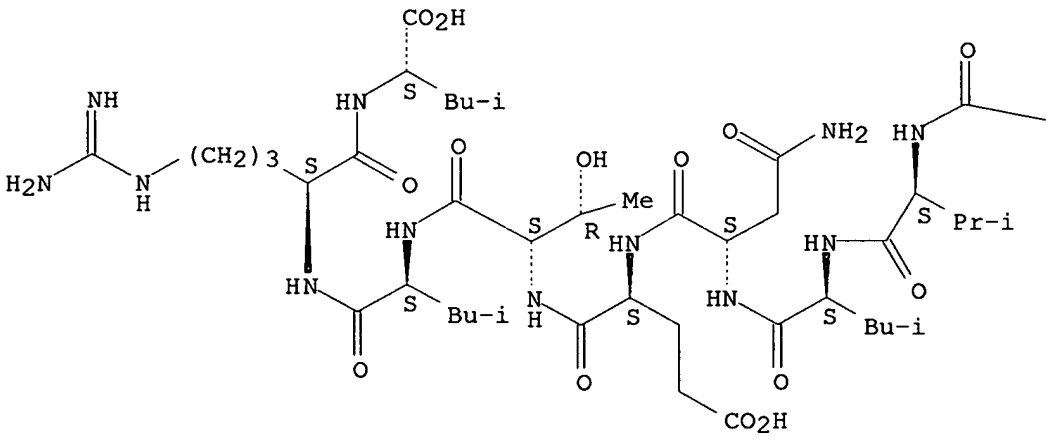
Absolute stereochemistry.

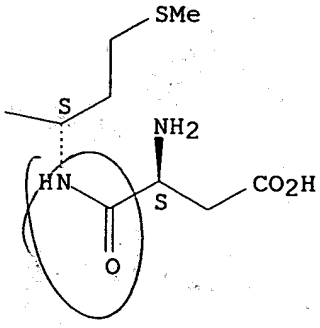


L24 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1996:240732 CAPLUS
DN 124:286416
TI Epitope mapping studies with human anti-cytochrome P450 3A antibodies. [Erratum to document cited in CA124:172880]
AU Leeder, S. J.; Gaedijk, A.; Lu, X.; Cook, V. A.
CS Can.
SO Molecular Pharmacology (1996), 49(4), 760
CODEN: MOPMA3; ISSN: 0026-895X
PB Williams & Wilkins
DT Journal
LA English
AB The errors were not reflected in the abstr. or the index entries.
IT **173791-50-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(epitope mapping of rat cytochrome P 450 3A1 for antibodies of humans with hypersensitivity to anticonvulsants (Erratum))
RN 173791-50-9 CAPLUS
CN L-Leucine, N-[N2-[N-[N-[N-[N2-[N-[N-(N-L-.alpha.-aspartyl-L-methionyl)-L-valyl]-L-leucyl]-L-asparaginyl]-L-.alpha.-glutamyl]-L-threonyl]-L-leucyl]-L-arginyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A




SMe
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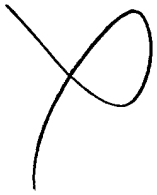
HN
S
CO2H
O



L24 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1996:177848 CAPLUS
DN 124:232269
TI Quinoline derivatives as tachykinin NK3 receptor antagonists
IN Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PA Smithkline Beecham Farmaceutici S.P.A., Italy
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9532948	A1	19951207	WO 1995-EP2000	19950523
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2191352	AA	19951207	CA 1995-2191352	19950523
	CA 2191352	C	20010130		
	CA 2257662	AA	19951207	CA 1995-2257662	19950523
	AU 9526164	A1	19951221	AU 1995-26164	19950523
	AU 699319	B2	19981203		
	HU 76286	A2	19970728	HU 1996-3262	19950523
	CN 1156451	A	19970806	CN 1995-194338	19950523
	CN 1092642	B	20021016		
	BR 9507788	A	19970923	BR 1995-7788	19950523
	EP 804419	A1	19971105	EP 1995-920894	19950523
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
	JP 10500697	T2	19980120	JP 1996-500287	19950523
	RO 114445	B3	19990430	RO 1996-2234	19950523
	EP 940391	A2	19990908	EP 1998-204483	19950523
	EP 940391	A3	19991110		
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	JP 2000026314	A2	20000125	JP 1999-172597	19950523
	NZ 329979	A	20000728	NZ 1995-329979	19950523
	RU 2155754	C2	20000910	RU 1996-124804	19950523
	JP 2002179594	A2	20020626	JP 2001-326622	19950523
	SK 282721	B6	20021106	SK 1996-1514	19950523
	SK 282722	B6	20021106	SK 1999-47	19950523
	ZA 9504269	A	19960514	ZA 1995-4269	19950525
	US 5811553	A	19980922	US 1995-450438	19950525
	TW 427977	B	20010401	TW 1995-84105319	19950526
	FI 9604712	A	19970123	FI 1996-4712	19961126
	NO 9605036	A	19970124	NO 1996-5036	19961126
	CN 1276211	A	20001213	CN 1999-100978	19990115
	AU 9912162	A1	19990325	AU 1999-12162	19990119
	FI 9900268	A	19990210	FI 1999-268	19990210
	NO 9901813	A	19970124	NO 1999-1813	19990416
PRAI	IT 1994-MI1099	A	19940527		
	IT 1995-MI494	A	19950314		
	AU 1995-26164	A3	19950523		

	CA 1995-2191352	A	19950523
	EP 1995-920894	A3	19950523
	JP 1996-500287	A	19950523
	NZ 1995-287442	A1	19950523
	WO 1995-EP2000	W	19950523

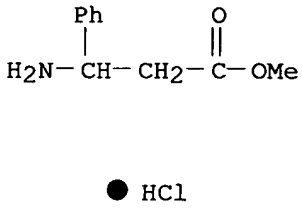
OS MARPAT 124:232269

AB NK3 receptor antagonists I [Ar = (un)substituted Ph, naphthyl, cycloalkadienyl, heteroaryl; R = (un)substituted alkyl, cycloalkyl, (un)substituted Ph, phenylalkyl, or heteroaryl, CO2H and derivs., etc.; R1, R2 = H, alkyl; or R1R2 = (CH2)3-5; or RR1 = (CH2)2-5; R3, R4 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, amino, etc.; R5 = alkyl, cycloalkyl, (un)substituted (hetero)aryl; X = O, S, N(CN)] are useful in treating pulmonary, CNS, and neurodegenerative disorders, etc. Approx. 115 compds. were prepd. For example, amidation of 3-methyl-2-phenylquinoline-4-carbonyl chloride with (R)-.alpha.-ethylbenzylamine gave title compd. II in 58% yield. II had IC50 of 5.6 nM for displacement of [3H]-senktide from guinea-pig cortical NK3 receptors. Antagonist activity of I was shown by inhibition of senktide-induced contraction of guinea-pig ileum.

IT **88831-43-0**, (R,S)-Methyl 3-amino-3-phenylpropionate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

RN 88831-43-0 CAPLUS

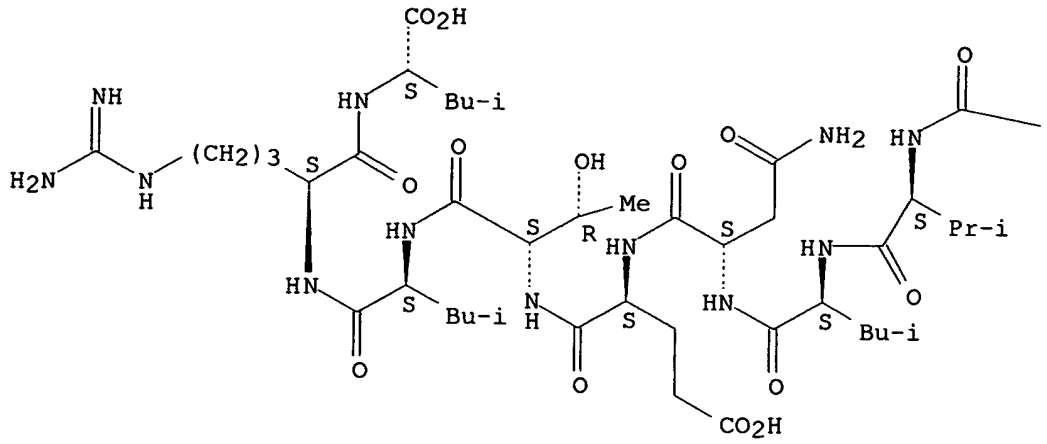
CN Benzenepropanoic acid, .beta.-amino-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



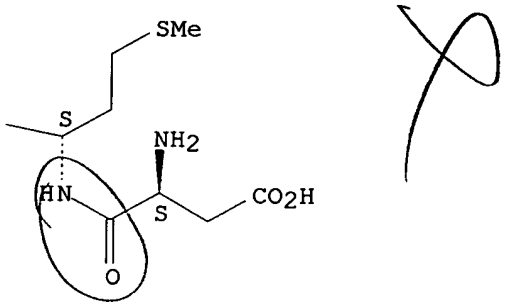
L24 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1996:117340 CAPLUS
DN 124:172880
TI Epitope mapping studies with human anti-cytochrome P450 3A antibodies
AU Leeder, J. Steven; Gaedigk, Andrea; Lu, Xiaoli; Cook, Vicki A.
CS Div. Clinical Pharmacology Toxicology, Res. Inst., Toronto, ON, M5G 1X8, Can.
SO Molecular Pharmacology (1996), 49(2), 234-43
CODEN: MOPMA3; ISSN: 0026-895X
PB Williams & Wilkins
DT Journal
LA English
AB A subset of patients with hypersensitivity reactions to the arom. anticonvulsants phenytoin, carbamazepine, and phenobarbital have circulating antibodies that recognize members of the rat cytochrome P 450 (CYP) 3A subfamily. These antibodies do not recognize related human CYP3A proteins despite the high degree of structural similarity. To investigate the relation between P 450-mediated drug metab. and the development of anti-P 450 antibodies, the authors initiated epitope mapping studies by screening a library of fusion proteins constructed from rat CYP3A1 with an anti-CYP3A1-pos. patients serum sample. Pos. signals from colony lifts were confirmed by SDS-PAGE and immunoblotting, and a 26-amino acid sequence corresponding to amino acids 342-367 of the CYP3A1 protein (NKAPPTYDTVMEMEYLDMVLNETLRL) was identified as contg. the epitope recognized by IgG3 antibodies in this serum sample. By subjecting inserts from two clones into a second round of library construction and screening by immunoblot anal., the authors further defined the epitope to EYLDMVLNETLRL. Single amino acid deletions identified DMVLNETLRL as the min. amino acid sequence required for antibody binding. The corresponding sequence in the four human CYP3A proteins differs by only one amino acid (DMVVNETLRL). This amino acid is crit. to antibody recognition as immunoreactivity of the L361V mutant is markedly reduced. Anti-CYP3A antibodies in nine of nine addnl. sera also recognized the 13-amino acid epitope; for five of these sera, the min. antibody binding sequence was DMVLNETLRL. The proximity of this epitope to a region detg. substrate specificity may provide the link among reactive metabolite prodn., hapten formation, and the prodn. of anti-P 450 antibodies in anticonvulsant-induced idiosyncratic reactions.
IT **173791-50-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(epitope mapping of rat cytochrome P 450 3A1 for antibodies of humans with hypersensitivity to anticonvulsants)
RN 173791-50-9 CAPLUS
CN L-Leucine, N-[N2-[N-[N-[N-[N2-[N-[N-(N-L-.alpha.-aspartyl-L-methionyl)-L-valyl]-L-leucyl]-L-asparaginyl]-L-.alpha.-glutamyl]-L-threonyl]-L-leucyl]-L-arginyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1995:629919 CAPLUS
DN 123:56559
TI Preparation of peptide analog cholecystokinin type B receptor agonists.
IN Shiosaki, Kazumi; Nadzan, Alex M.; Garvey, David S.; Shue, Youe-Kong; Brodie, Mark S.; Holladay, Mark W.; Chung, John Y.-L.; Tufano, Michael D.; May, Paul D.
PA Abbott Laboratories, USA
SO U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 791,805, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

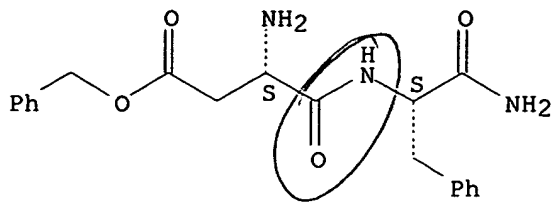
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5340802	A	19940823	US 1993-11055	19930129
PRAI	US 1989-375107		19890630		
	US 1990-531771		19900606		
	US 1991-791805		19911113		

OS MARPAT 123:56559
AB W-Y-Z [W = Q1, Q2, A-B; A = R7CH2CHR6CO, R2R8D, Q3, Q4, etc.; B = NR3CH(CH2R13)CO, Q5; Y = NHCH(CH2R16)CO; Z = NR3CH(CH2R17)COR18, Q6, etc.; R1 = alkyl, hydroxyalkyl, monosubstituted alkylene; R2 = (substituted) naphthyl, benzoheterocyclyl; R3 = H, alkyl; R4 = H, protecting group; R5 = C2-4 alkylene; R6 = H, halo, OH, alkoxy, thioalkoxy, amino, etc.; R7 = (substituted) naphthyl, Ph, benzohet, heterotricyclyl, carbotricyclyl, etc.; R8 = alkylene, alkenylene; D = null, CO; R11 = H, OH, halo, alkyl, amino, monosubstituted alkylene; R12 = H, alkyl, alkanoyl; R13 = alkyl, monosubstituted alkylene; R14 = null, O, S; R15 = H, alkyl, alkoxy, thioalkoxy, monosubstituted alkylene; R16 = CO2H, tetrazolyl; R17 = alkyl, cycloalkyl, (substituted) heterocyclyl, naphthyl, Ph, benzoheterocyclyl; R18 = NHR24, NHNHR3; R19-R22 = H, alkyl, halo, haloalkyl, alkoxy, thioalkoxy, OH, alkoxycarbonyl, CO2H, NO2, amino, OSO3H, etc.; R24 = H, OH, alkyl, alkoxy; with provisos], were prepd. Thus, Ctp-Tpp-Asp-.alpha.-Nal-NH2 [Ctp = Q3 (R11, R12 = H), Tpp = Q7; .alpha.-Nal = 3-(1-naphthyl)alanyl] (soln. phase prepn. given) showed IC50 = 0.4 nM and 1,400 nM for binding to cortex (type B) and pancreas (type A) cholecystokinin receptors, resp.
IT **60058-91-5 164007-41-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptide analog cholecystokinin type B receptor agonists)
RN 60058-91-5 CAPLUS
CN L-Phenylalaninamide, L-.alpha.-aspartyl-, phenylmethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

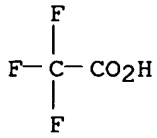
CRN 5609-55-2
CMF C20 H23 N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

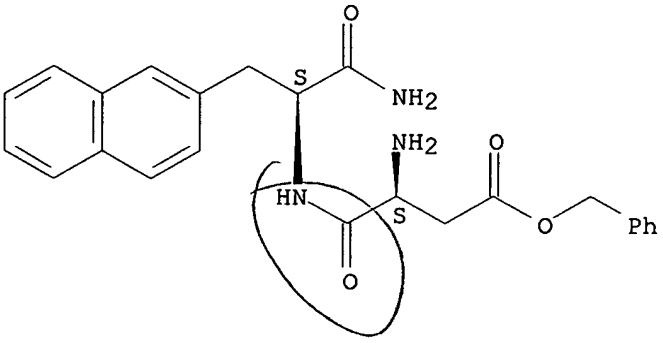


RN 164007-41-4 CAPLUS
CN L-Alaninamide, L-.alpha.-aspartyl-3-(2-naphthalenyl)-, phenylmethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

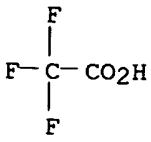
CRN 164007-40-3
CMF C24 H25 N3 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



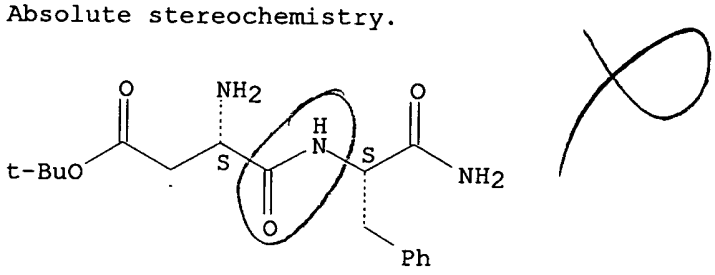
IT **14433-22-8P 131450-72-1P 134676-45-2P**
134676-47-4P 164006-94-4P 164007-11-8P
164007-21-0P 164007-43-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide analog cholecystokinin type B receptor agonists)

RN 14433-22-8 CAPLUS
CN L-Phenylalaninamide, L-.alpha.-aspartyl-, 1,1-dimethylethyl ester, monoacetate (9CI) (CA INDEX NAME)

CM 1

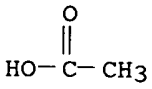
CRN 5241-67-8
CMF C17 H25 N3 O4

Absolute stereochemistry.



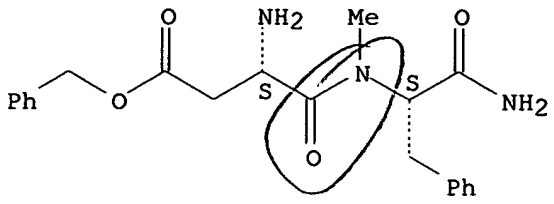
CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 131450-72-1 CAPLUS
CN L-Phenylalaninamide, L-.alpha.-aspartyl-N.alpha.-methyl-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

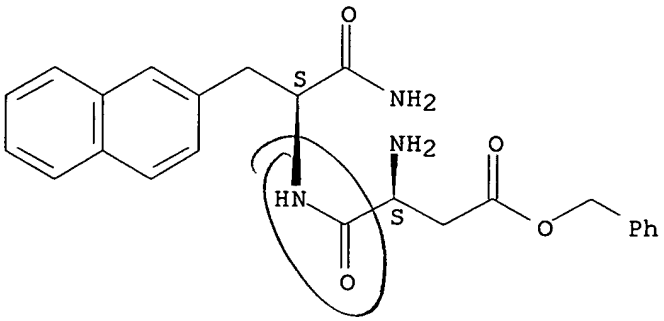
Absolute stereochemistry.



● HCl

RN 134676-45-2 CAPLUS
CN L-Alaninamide, L-.alpha.-aspartyl-3-(2-naphthalenyl)-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



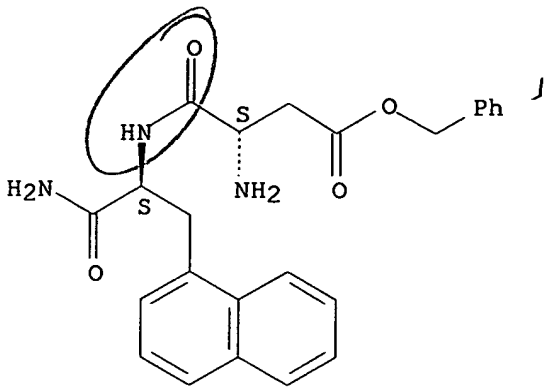
● HCl

RN 134676-47-4 CAPLUS
CN L-Alaninamide, L-.alpha.-aspartyl-3-(1-naphthalenyl)-, phenylmethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

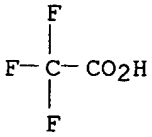
CRN 134676-46-3
CMF C24 H25 N3 O4

Absolute stereochemistry.



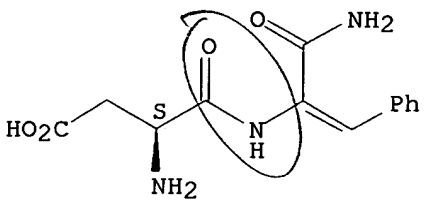
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 164006-94-4 CAPLUS
CN Phenylalaninamide, L-.alpha.-aspartyl-.alpha.,.beta.-didehydro-, monohydrochloride (9CI) (CA INDEX NAME)

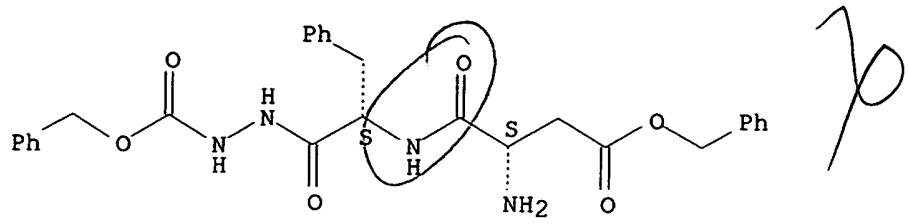
Absolute stereochemistry.
Double bond geometry unknown.



● HCl

RN 164007-11-8 CAPLUS
CN L-Phenylalanine, N-L-.alpha.-aspartyl-, 4-(phenylmethyl) ester, 1-[2-[(phenylmethoxy)carbonyl]hydrazide], monohydrochloride (9CI) (CA INDEX NAME)

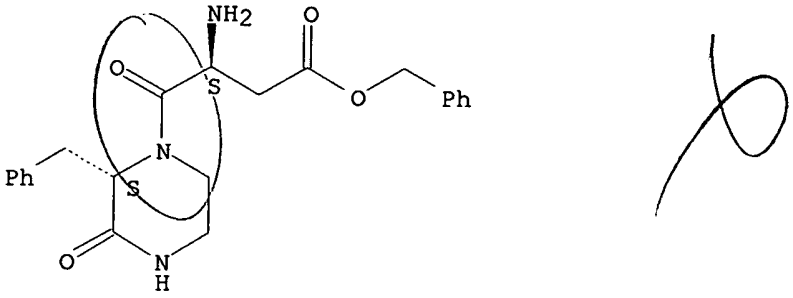
Absolute stereochemistry.



● HCl

RN 164007-21-0 CAPLUS
CN 1-Piperazinebutanoic acid, .beta.-amino-.gamma.,3-dioxo-2-(phenylmethyl)-, phenylmethyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

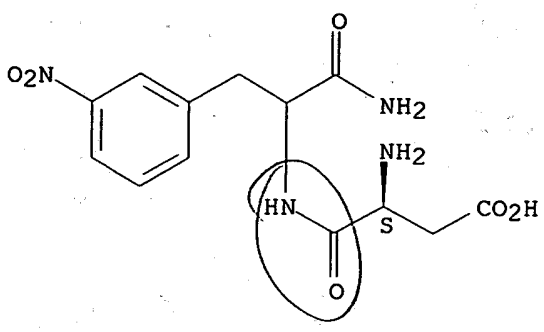
Absolute stereochemistry.



● HCl

RN 164007-43-6 CAPLUS
CN Phenylalaninamide, L-.alpha.-aspartyl-3-nitro-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L24 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1995:397398 CAPLUS
DN 122:205212
TI Use of L-carnitine or acyl-L-carnitines and valproate for treating seizure disorders
IN Cavazza, Claudio
PA Sigma-Tau Industrie Farmaceutiche Riunites S.p.A., Italy
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

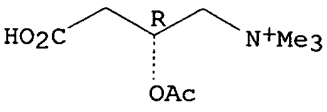
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 637449	A1	19950208	EP 1994-830306	19940622
	EP 637449	B1	19980107		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 161718	E	19980115	AT 1994-830306	19940622
	ES 2111891	T3	19980316	ES 1994-830306	19940622
PRAI	IT 1993-RM441		19930706		

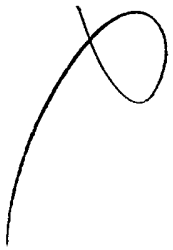
AB The coordinated use of L-carnitine or acyl-L-carnitines and valproate allows a dramatic decrease in seizure frequency to be obsd. in epileptic patients.
IT **99581-13-2**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of L-carnitine or acyl-L-carnitines and valproate for treating seizure disorders)
RN 99581-13-2 CAPLUS
CN L-Aspartic acid, ion(1-), (2R)-2-(acetyloxy)-3-carboxy-N,N,N-trimethyl-1-propanaminium (9CI) (CA INDEX NAME)

CM 1

CRN 89946-58-7
CMF C9 H18 N O4

Absolute stereochemistry. Rotation (-).

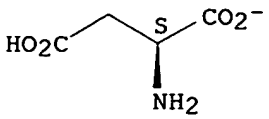




CM 2

CRN 44809-12-3
CMF C4 H6 N O4

Absolute stereochemistry.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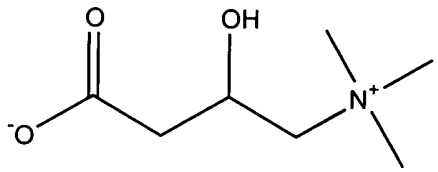
CO2−
NH2



L-carnitine

Caution: Stereochemical terms discarded: l

(19) Europäisches Patentamt
European Patent Office
Office uropéen des brevets

(11) Publication number : **0 637 449 A1**

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number : **94830306.0**

(22) Date of filing : **22.06.94**

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(30) Priority : **06.07.93 IT RM930441**

(43) Date of publication of application : **08.02.95 Bulletin 95/06**

(84) Designated Contracting States : **AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE**

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(54) Use of L-carnitine or acyl L-carnitines and valproate for treating seizure disorders.

(57) The co-ordinated use of L-carnitine or acyl L-carnitines and valproate allows a dramatic decrease in seizure frequency to be observed in epileptic patients.

EP 0 637 449 A1

The present inventi n relates to a novel therapeutical use of L-carnitine, some acyl L-carnitines and th ir pharmacologically acceptable salts for treating seizure disorders (pil psy).

More specifically, the present inv ntion relates to the coordinated use of L-carnitine, acyl L-carnitines or their pharmacologically acceptable salts and valproate (i.e. a pharmacologically acceptable salt of valproic acid, such as sodium or magnesium valproate) for decreasing the seizure frequency in epileptic patients.

Within the scope of the present invention, by "coordinated use" of the aforesaid compounds it is meant indifferently both the co-administration, i.e. the substantially concomitant supplementation of L-carnitine or acyl L-carnitine or a pharmacologically acceptable salt thereof and valproate, as active ingredients, and the administration of a combination preparation containing a mixture of the aforesaid active ingredients, in addition to suitable excipients, if any.

L-carnitine supplementation concomitantly administered with valproate therapy in epileptic patients, particularly epileptic young children, has been already disclosed although the therapeutical effect aimed at does not allow the novel use, object of the present invention, to be in any way foreseen.

Valproate is a remarkably efficacious anticonvulsant; however, in some cases it can cause a severe or fatal hepatotoxicity. Valproate interferes with carnitine metabolism and this is the cause of valproate toxicity.

As known, carnitine performs two basic physiologic functions. First, it carries long-chain fatty acids across the inner mitochondrial membrane into the mitochondrion matrix where the beta-oxidation takes place. Secondly, carnitine helps to regulate the intramitochondrial ratio of acyl CoA to free CoA. Acyl carnitine transferase located on the inner wall of inner mitochondrial membrane favours the binding of carnitine to acylCoA forming acylcarnitine esters for transport out of the mitochondrion.

The same reaction releases and makes available the CoA within the mitochondrion. This carnitine function is essential since it removes excessive (and potentially toxic) short and medium chain fatty acids from the mitochondrion, maintaining sufficient free CoA within the mitochondrion to provide adequate cell energy metabolism.

Tissue (mitochondrial) carnitine deficiency affects the energy metabolism by hindering the beta-oxidation of long-chain fatty acids, allowing the accumulation of acyl CoA in mitochondria to occur, which results in lower amounts of free CoA to be available.

This endangers the activities of those tissues and rgans, such as the muscular tissue and th brain, which are most heavily depend nt n mitoch ndrial energy metabolism, and brings about th nset of the symptoms and signs of ncephalopathy and myopathy.

Also liver dysfunctions can result from reduced mitochondrial metabolism in th liver and the release of hepatotoxic m tabolites in th blood stream.

A number of causes may lead to even severe carnitine deficiencies in epileptic patients. The most frequent causes include inborn metabolic disorders, inappropriate dietary intake and medication with anticonvulsant drugs.

Among these drugs, valproate exerts a potent effect on carnitine-linked metabolism. Indeed, valproic acid (2-propylpentanoic acid), a short-chain fatty acid, combines with carnitine in mitochondria forming valproylcarnitine for transport out of mitochondria and excretion into urine.

In 1982, Othani et al (Othani et al., Carnitine deficiency and hyperammonemia associated with valproate therapy, J. Pediatr. 1982; 101: 782-785) were the first Authors who detected carnitine deficiency in valproate-treated patients.

Already in 1981, Haas et al (Haas R. et al., Inhibitory effects of sodium valproate on oxidative phosphorylation, Neurology 1981; 31: 1473-1476) had shown valproate toxicity towards mitochondria of rat liver in vitro, subsequently shown also in vivo (Sugimoto et al., Hepatotoxicity in rat following administration of valproic acid: effect of L-carnitine supplementation, Epilepsia 1987; 28: 373-377).

Furthermore, valproate can inhibit mitochondrial beta-oxidation of long-chain fatty acids via two mechanisms. The first is the formation of valproyl-CoA which sequesters free CoA thus decreasing its availability for fatty acid metabolism. The second, even more importantly, is the inhibition of the enzymes which play a role in beta-oxidation by some valproate metabolites, notably 4-en valproate.

It was furthermore found that the administration of anticonvulsants can cause severe to fatal hepatotoxicity, particularly in young children.

For this reason, some Authors (see e.g. David L. Coulter, Prevention of hepatotoxicity recurrence with valproate monotherapy and carnitine, [abstract] Ann. Neurol. 1988, 24: 301) have proposed a clinical protocol providing an antiepileptic valproate monotherapy with concomitant carnitine administration. This Author concludes: "These results suggest that children with previous hepatotoxic reactions to valproate may tolerate the drug without recurrence of hepatotoxicity when this protocol is used. Valproate monotherapy with carnitine supplementation could allow more children to benefit from this drug".

It has now been found that the co-ordinated use of L-carnitine or an acyl L-carnitine wherein the acyl group has 2-8, preferably 2-6, carbon atoms or their pharmacologically acceptabl salts and a pharmacologically acceptabl salt of valproic acid dramatically decreases the seizure frequ ncy in epileptic patients.

This remarkabl therapeutical result could not be

anticipated on the ground of the aforesaid known efficacy of L-carnitine in decreasing valproate hepatotoxicity.

The present inv ntion, therefore, relates to the use of L-carnitine or an acyl L-carnitin wherein the acyl group has 2-8, preferably 2-6, carbon atoms or their pharmacologically acceptable salts and a pharmacologically acceptable salt of valproic acid for producing a medicament for decreasing the seizure frequency in epileptic patients.

Preferably, the acyl L-carnitine is selected from acetyl, propionyl, butyryl, valeryl and isovaleryl L-carnitine.

The pharmacologically acceptable salt of L-carnitine and acyl L-carnitine is selected from chloride, bromide, orotate, acid aspartate, acid citrate, acid phosphate, fumarate and acid fumarate, lactate, maleate and acid maleate, acid oxalate, acid sulphate, glucosephosphate, tartrate and acid tartrate.

Among the pharmacologically acceptable salts, the respective inner salts are included.

Examples of pharmacologically acceptable salts of valproic acid are sodium valproate and magnesium valproate.

The present invention also provides a pharmaceutical composition (combination preparation) for decreasing the seizure frequency in epileptic patients which comprises L-carnitine, an acyl-L-carnitine wherein the acyl group is a linear or branched acyl having 2-8, preferably 2-6, carbon atoms or a pharmacologically acceptable salt thereof and a pharmacologically acceptable salt of valproic acid as active ingredients.

Preferred examples of acyl L-carnitines, pharmacologically acceptable salts of L-carnitine, acyl L-carnitines and valproic acid salts are those previously indicated.

A suitable pharmaceutical composition in unit dosage form comprises from about 0.3 to about 0.5 g of L-carnitine or an equivalent amount of acyl L-carnitine or a pharmacologically acceptable salt thereof and from about 0.2 to about 0.5 g of sodium valproate or magnesium valproate.

The efficacy of the co-ordinated use of L-carnitine (or acyl L-carnitines) and valproate for decreasing the seizure frequency in epileptic patients has been tested in several clinical trials. One of these trials is described in detail hereinbelow.

CLINICAL TRIAL

Fortyfive patients, 20 females and 25 males, mean age 24.5±8.48 years, were included in the study.

The patients xhibited the following seizure types:

g neralized tonic cl nic
partial simpl
partial complex
absence
atonic
tonic
L nnox Gastaux

Some patients had more than one seizure type.

All of the patients had been treated only with valproate for at least six months.

Subsequently, they were treated with both valproate and L-carnitine for at least one year.

At intervals L-carnitine activity was assessed on some parameters including seizure frequency, in comparison with the pre-treatment period (valproate only, no L-carnitine). The intervals selected for all the controls were: between the start to 6 months of L-carnitine therapy, 6 months of L-carnitine therapy, and L-carnitine therapy greater than 12 months.

Parameter assessment was not carried out at prefixed dates but within the 0-6, 6-12 and greater than 12 month periods in order to evaluate the seizure frequency over a sufficiently extended time period.

SEIZURE FREQUENCY:

Following L-carnitine treatment, the seizure frequency decreased progressively and steadily with respect to the pre-treatment period.

- Pre-carnitine period vs greater than 12 months L-carnitine period, $p<0.001$;
- Start-6 months vs greater than 12 months L-carnitine period, $p=0.0001$;
- 6-12 months vs greater than 12 months L-carnitine period, $p=0.0001$.

The effect was most pronounced after the first 6 months of L-carnitine therapy and continued to enhance after 1 year of L-carnitine therapy. The effect appeared to be independent on valproate dosage and serum concentration.

Claims

1. Use of L-carnitine or an acyl L-carnitine wherein the acyl group has 2-8, preferably 2-6, carbon atoms or their pharmacologically acceptable salts and a pharmacologically acceptable salt of valproic acid for decreasing the seizure frequency in epileptic patients.

2. Use of L-carnitine or an acyl L-carnitine wherein the acyl group has 2-8, preferably 2-6, carbon atoms or their pharmacologically acceptable salts and a pharmacologically acceptable salt of valproic acid for producing a medicament for decreasing th seizure frequency in epil ptic pati nts.

3. Th use of claims 1 or 2 wherein the acyl L-car-

nitine is selected from acetyl, propi nyl, butyryl, valeryl and isovaleryl L-carnitine.

4. The us of claims 1, 2 or 3 wh rein the pharmacologically acceptabl salt of L-carnitin or acyl L-carnitine is selected from the inner salt, chloride, bromide, orotate, acid aspartate, acid citrate, acid phosphate, fumarate and acid fumarate, lactate, maleate and acid maleate, acid oxalate, acid sulphate, glucosephosphate, tartrate and acid tartrate.

5. The use according to anyone of the preceding claims wherein the pharmacologically salt of valproic acid is selected from sodium valproate and magnesium valproate.

6. A pharmaceutical composition for decreasing the seizure frequency in epileptic patients which comprises L-carnitine, an acyl L-carnitine wherein the acyl group is a linear or branched acyl having 2-8, preferably 2-6, carbon atoms or a pharmacologically acceptable salt thereof and a pharmacologically acceptable salt of valproic acid.

7. The pharmaceutical composition of claim 6 wherein the acyl L-carnitine is selected from acetyl, propionyl, butyryl, valeryl and isovaleryl L-carnitine and the pharmacologically salt of valproic acid is selected from sodium valproate and magnesium valproate.

8. The pharmaceutical composition of claims 6 or 7 in unit dosage form comprising from about 0.3 to about 0.5 g of L-carnitine or an equivalent amount of acyl L-carnitine or a pharmacologically acceptable salt thereof and from about 0.2 to about 0.5 g of sodium valproate or magnesium valproate.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 83 0306

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	DE-A-37 26 945 (H. DIETL) * the whole document * ---	1-8	A61K31/205 //(A61K31/205, 31:20)
D,X, Y	EPILEPSIA vol. 28 , 1987 pages 373 - 377 T. SUGIMOTO ET AL. 'Hepatoxicity in rat following administration of valproic acid: Effect of L-carnitine supplementation' * the whole document * ---	1-8	
D,X, Y	ANN. NEUROL vol. 24 , 1988 page 301 D. COULTER 'Prevention of hepatoxicity recurrence with valproate monotherapy and carnitine' * abstract * ---	1-8	
Y	INT. PEDIATR. vol. 5, no. 1 , 1990 pages 54 - 57 M. CASTRO-GAGO ET AL. 'Effects of valproic acid on the urea cycle and carnitine metabolism' * page 54 * ---	1-8	TECHNICAL FIELDS SEARCHED (Int.Cl.6) A61K
Y	PEDIATR. RES. vol. 31, no. 4PT1 , April 1992 page 419 J. HOLOWACH ET AL. 'Amelioration of adverse effects of valproic acid on ketogenesis and liver coenzyme A metabolism by cotreatment with pantothenate and carnitine in developing mice: Possible clinical significance' * the whole document * ---	1-8	
	-/--		

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	30 September 1994	Foerster, W

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 83 0306

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	PHARMACOL. TOXICOL. vol. 72, no. 3 , March 1993 pages 145 - 147 M. MATSUOKA ET AL. 'Effects of L and D-carnitine on brain energy metabolites in mice given sublethal doses of ammonium acetate' * abstract *	1-8	
Y	BRAIN RES. vol. 567, no. 2 , 1991 pages 328 - 331 M. MATSUOKA ET AL. 'Suppression of neurotoxicity of ammonia by L-carnitine' * page 330 *	1-8	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	30 September 1994	Foerster, W

CATEGORY OF CITED DOCUMENTS

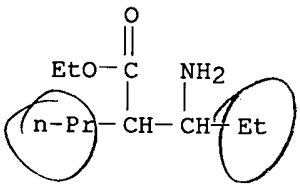
X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

L24 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1994:605927 CAPLUS
DN 121:205927
TI Synthesis and evaluation of amino analogs of valproic acid
AU Scott, K. R.; Adesioye, Sandra; Ayuk, Patricia B.; Edafiogho, Ivan O.; John, Dolly; Kodwin, Patrick; Maxwell-Irving, Thomasena; Moore, Jacqueline A.; Nicholson, Jesse M.
CS Coll. Pharm. Pharm. Sci., Howard Univ., Washington, DC, 20059, USA
SO Pharmaceutical Research (1994), 11(4), 571-4
CODEN: PHREEB; ISSN: 0724-8741
DT Journal
LA English
AB Valproic acid, an **antiepileptic** drug, is extensively metabolized in humans. Two putative metabolites, 2-propyl-3-aminopentanoic acid (3-aminovalproic acid) and 2-propyl-4-aminopentanoic acid (4-aminovalproic acid), which may result from the transamination of the resp. keto acids may explain the unusual extended seizure protection elicited by valproic acid. The title compds. were synthesized as their racemic Et esters and submitted for anticonvulsant evaluation by the **antiepileptic** drug development program of the Natl. Inst. of Neurol. and Communicative Disorders and Stroke. The results verified the authors' hypothesis, as Et 4-amino-2-propylpentanoate was active in the s.c. pentylenetetrazol evaluation at 30 mg/kg. Both esters were highly toxic at 300 mg/kg.
IT **158038-40-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., toxicity, anticonvulsant activity of)
RN 158038-40-5 CAPLUS
CN Pentanoic acid, 3-amino-2-propyl-, ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1994:116847 CAPLUS
DN 120:116847
TI Biodegradable controlled release melt-spun delivery system
IN Fuisz, Richard C.
PA Fuisz Technologies, Ltd., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

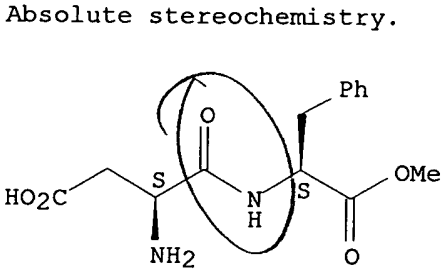
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9324154	A1	19931209	WO 1993-US5307	19930602
	W: AU, CA, HU, JP, KR, PL, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5518730	A	19960521	US 1992-893238	19920603
	AU 9344058	A1	19931230	AU 1993-44058	19930602
	AU 665844	B2	19960118		
	JP 07507548	T2	19950824	JP 1994-500877	19930602
	EP 746342	A1	19961211	EP 1993-914373	19930602
	EP 746342	B1	20020814		
	R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
PRAI	US 1992-893238	A2	19920603		
	WO 1993-US5307	A	19930602		

AB Biodegradable controlled-release delivery systems using melt-spun biodegradable polymers as carriers for bio-effecting agents such as pharmaceutical actives are disclosed. Oral dose forms as well as implants are described. For example, polyglycolide was melt-spun in combination with various drugs such as vancomycin, gentamicin, tolmetin, diphenhydramine, ibuprofen, and insulin and controlled drug release was demonstrated.

IT **22839-47-0**, Aspartame
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release pharmaceuticals formed by flash-flow melt-spinning contg., biodegradable polymers as carriers in)

RN 22839-47-0 CAPLUS
CN L-Phenylalanine, L-.alpha.-aspartyl-, 2-methyl ester (9CI) (CA INDEX NAME)

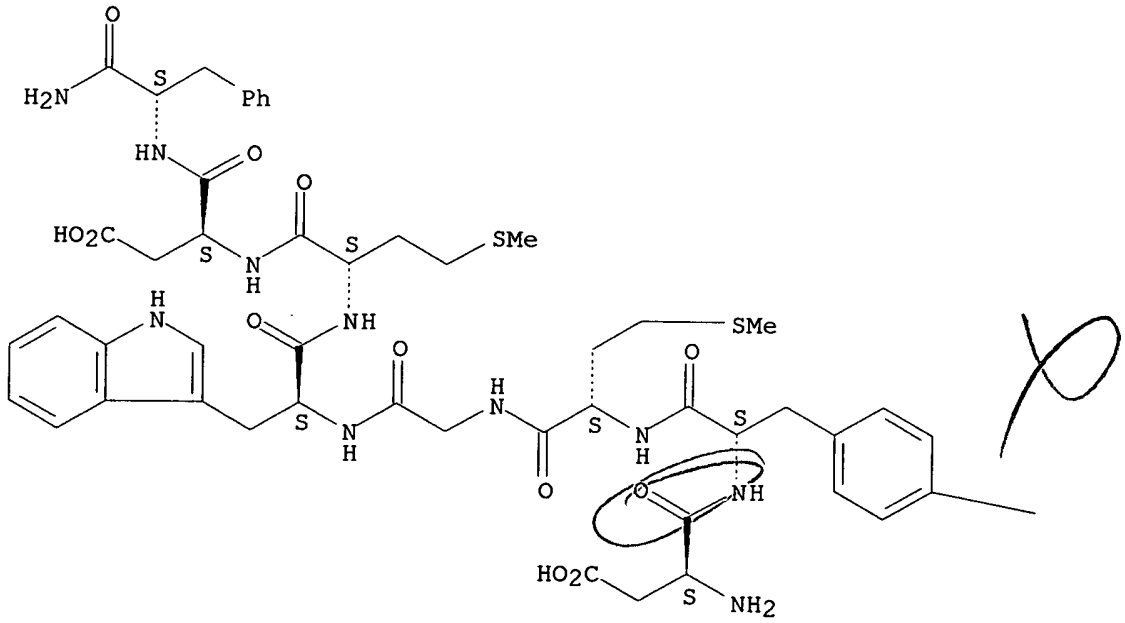
Absolute stereochemistry.

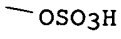


L24 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1993:641682 CAPLUS
DN 119:241682
TI Effect of CCK-8 on audiogenic epileptic seizure in P77PMC rats
AU Zhang, L. X.; Zhou, Y.; Du, Y.; Han, J. S.
CS Neurosci. Res. Cent., Beijing Med. Univ., Beijing, 100083, Peop. Rep. China
SO Neuropeptides (Edinburgh, United Kingdom) (1993), 25(1), 73-6
CODEN: NRPPDD; ISSN: 0143-4179
DT Journal
LA English
AB P77PMC rat is a breed of rat with congenital audiogenic seizure (AS). AS attacks were suppressed by cholecystokinin octapeptide (CCK-8) injected i.p. at a dose of 50 .mu.g/kg, but not at 25 .mu.g/kg. RIA study showed that the CCK-8 immunoreactivity in the cerebral cortex and hippocampus is much lower in P77PMC rats than that of Wistar rats. The results suggest that a low cerebral content of CCK-8 may account for the high susceptibility to AS in P77PMC rats.
IT **25126-32-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, in audiogenic seizures)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



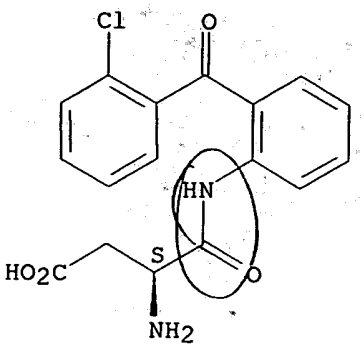


L24 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1993:101995 CAPLUS
DN 118:101995
TI Preparation of 1- or 3-substituted chlonazepam derivatives as haptens and antigens for immunoassay of chlonazepam
IN Kanehiro, Masahiko; Akita, Tatsuo; Yajima, Ryuichi; Kumagai, Yasuyuki; Nakaya, Miho
PA Dainabot Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 04202186	A2	19920722	JP 1990-330156	19901130
PRAI JP 1990-330156		19901130		

OS MARPAT 118:101995
AB The title compds. [I; one of R1, R2 = H, the other = RZQ; R = C1-10 linkage group contg. a hetero atom and a linear or branched chain contg. .ltoreq.10 heteroatoms in which .gtoreq.2 of the hetero atoms are not directly bonded to each other; Z = CO, C:NH, NH, NMe, N:N, SO2, CH2; Q = H, HO, halo, acyloxy, N-succinylimidoxy, N-phthalimidoxy, alkoxy, (un)substituted PhO, N-imidazolyl, 1-benzotriazolyloxy, polyamino acid or its deriv., or other antigen carrier, labeled compd.] are prepd. as antigens for enzyme immunoassay, RIA, and fluorescence immunoassay of chlonazepam in the treatment plan using chlonazepam as an anticonvulsant. Preferred compds. are I (Q = bovine serum albumin, fluorescent substance, fluorescein, enzyme, radioactive material). Thus, 108 mg chlonazepam was stirred with MeONa in MeOH-DMF at room temp., thereto 276 .mu.L BrCH2CO2CMe3 was added, and the mixt. was stirred overnight at room temp. to give 88% I (R1 = CH2CO2CMe3, R2 = H) which was treated with 50% CF3CO2H in CH2Cl2 to give 90% (R1 = CH2CO2H, R2 = H). This (37.4 mg) was esterified with N-hydroxysuccinimide in the presence of DCC in DMF-dioxane to give an active ester soln. which was reacted with aq. soln. of 110 mg bovine serum albumin adjusted to pH 8.5 with 0.1N NaOH while maintaining the same pH to give, after dialysis and freeze dry, antigen I (R1 = CH2CO2Q, Q = bovine serum albumin, R2 = H). Inoculation of mice with this antigen produced anti-chlonazepam monoclonal antibody which showed cross-reactivity 100, <0.1, and 20% to chlonazepam, metabolites 7-aminochlonazepam, and 3-hydroxychlonazepam, resp.
IT **145741-39-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for hapten and antigen for immunoassay of chlonazepam)
RN 145741-39-5 CAPLUS
CN Butanoic acid, 3-amino-4-[[2-(2-chlorobenzoyl)phenyl]amino]-4-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


Cl
O
HN
S
HO2C
O
NH2

L24 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1992:483456 CAPLUS
DN 117:83456
TI Controlling glutamine/glutamate-related neuronal injury
IN Rosenberg, Paul A.
PA Children's Medical Center Corp., USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

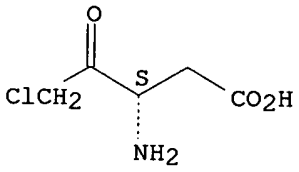
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9207562	A1	19920514	WO 1991-US8079	19911029
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5158976	A	19921027	US 1990-605528	19901029
	AU 9189297	A1	19920526	AU 1991-89297	19911029
PRAI	US 1990-605528		19901029		
	WO 1991-US8079		19911029		

AB Neuronal injury or death in a patient is inhibited with an effective amt. of an inhibitor of the enzymic conversion of glutamine to glutamate. The method is useful for treatment of Alzheimer's disease, epilepsy, amyotropic lateral sclerosis, etc. The inhibitor is e.g. azaserine, .alpha.-aminoadipic acid, azotomycin, or albizzen. A neuronal culture method for screening for inhibitors of neuronal injury and death is also disclosed.

IT **85985-02-0**
RL: BIOL (Biological study)
(as glutaminase inhibitor, for inhibition of neuronal injury or death)

RN 85985-02-0 CAPLUS
CN Pentanoic acid, 3-amino-5-chloro-4-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

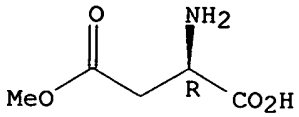


L24 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1992:255489 CAPLUS
DN 116:255489
TI Preparation and carboxypyrrolidinyl- and -piperidinylcarbonylmethylphospho nates as N-methyl-D-aspartate (NMDA) antagonists
IN Whitten, Jeffrey P.
PA Merrell Dow Pharmaceuticals, Inc., USA
SO Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 457324	A1	19911121	EP 1991-107955	19910516
	EP 457324	B1	19951206		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5194430	A	19930316	US 1991-675156	19910328
	CA 2042473	AA	19911118	CA 1991-2042473	19910513
	CA 2042473	C	20020101		
	ZA 9103604	A	19920226	ZA 1991-3604	19910513
	AU 9176498	A1	19911121	AU 1991-76498	19910514
	AU 641657	B2	19930930		
	IL 98148	A1	19961016	IL 1991-98148	19910515
	FI 9102382	A	19911118	FI 1991-2382	19910516
	FI 97388	B	19960830		
	FI 97388	C	19961210		
	NO 9101916	A	19911118	NO 1991-1916	19910516
	CN 1056499	A	19911127	CN 1991-103185	19910516
	CN 1027695	B	19950222		
	HU 59150	A2	19920428	HU 1991-1649	19910516
	HU 208831	B	19940128		
	AT 131172	E	19951215	AT 1991-107955	19910516
	ES 2083478	T3	19960416	ES 1991-107955	19910516
	JP 08012691	A2	19960116	JP 1991-140636	19910517
	JP 2977950	B2	19991115		
	US 5470844	A	19951128	US 1993-159913	19931130
PRAI	US 1990-525290	A	19900517		
	US 1991-675156	A	19910328		
	US 1992-986222	B1	19921207		

OS MARPAT 116:255489
AB AC(:M)CH2P(O)(OR1)2 [R1 = H, alkyl, CF3; M = O, NOR4, NNHR4; R4 = H, alkyl(phenyl); A = carboxypyridinyl and -pyrrolidinyl residues Q1-Q4; R2 = R1, cycloalkyl, trialkylamino, alkylphenyl, (substituted) Ph; R3, R6 = H, alkyl(phenyl), Ph, cyclohexylmethyl; R5 = H, alkyl(phenyl)], were prepd. as NMDA antagonists (no data). Thus, pyridine-2,3-dicarboxylic acid was reduced with Ni/Al in aq. NaOH to give piperidine-2,3-dicarboxylic acid. The latter was treated with PhCH2O2CCl to give the N-protected material as a cis/trans mixt. This was refluxed with Ac2O to give the anhydride, which was condensed with lithiated MeP(O)(OEt)2. The resulting 2-acid was converted to the benzyl ester and this was refluxed in 6N HCl to give title compd. I, which could be sepd. into the constituent isomers by chromatog.
IT **22728-89-8P 138738-52-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for methylaspartate antagonists)
RN 22728-89-8 CAPLUS
CN D-Aspartic acid, 4-methyl ester, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



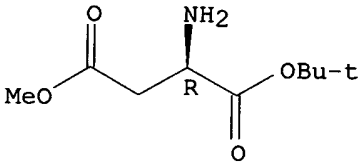
● HCl

RN 138738-52-0 CAPLUS
CN D-Aspartic acid, 1-(1,1-dimethylethyl) 4-methyl ester, acetate (9CI) (CA INDEX NAME)

CM 1

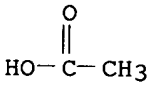
CRN 133637-94-2
CMF C9 H17 N O4

Absolute stereochemistry.



CM 2

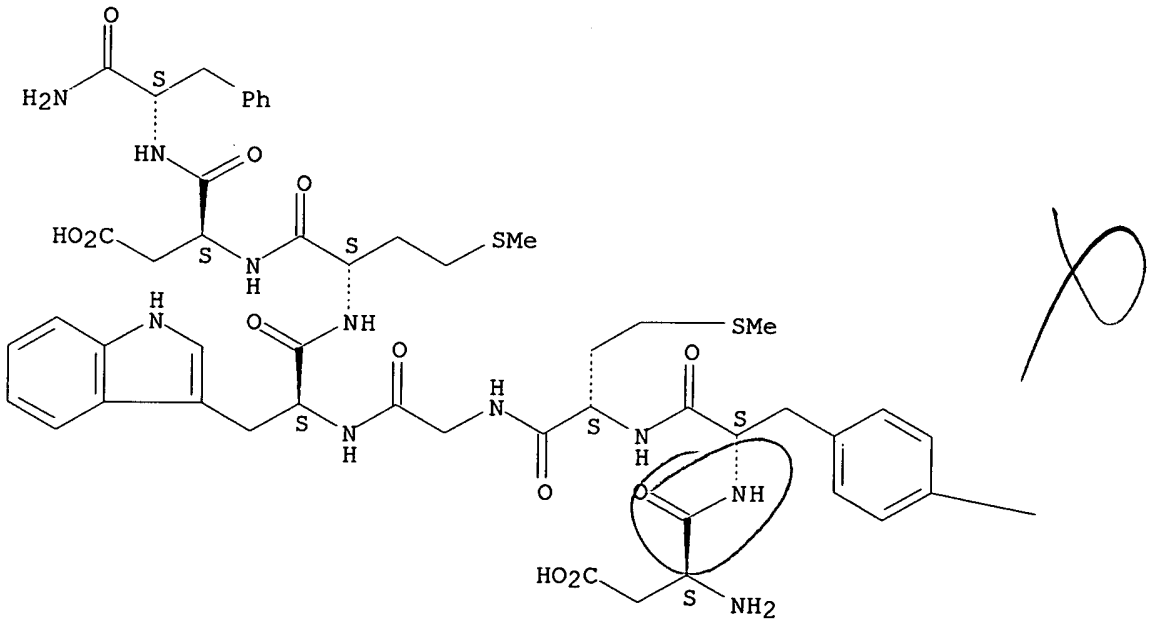
CRN 64-19-7
CMF C2 H4 O2



L24 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1992:144069 CAPLUS
DN 116:144069
TI CCK analogs containing non-coded amino acids
AU Toth, Gabor; Zarandi, Marta; Kovacs, Kalman
CS Orvosi Vegytani Int., Szegedi Orvostud. Egy., Szeged, H-6720, Hung.
SO Kemiai Kozlemenyek (1991), 72(2), 255-62
CODEN: KEKOAS; ISSN: 0022-9814
DT Journal
LA Hungarian
AB Six tetragastrin, pentagastrin and CCK-8 analogs, prepd. by known methods, were tested i.v. for gastrin activity (gastric HCl release) in rats, for cholecystokinin activity, on the rabbit gall bladder in vitro, and for anticonvulsant activity. The CCK-8 analog contg. p-sulfophenylalanine instead of aspartic acid, showed no gastrin or cholecystokinin activity, whereas its anticonvulsant activity was similar to that of CCK-8. The pentagastrin analog contg. tyrosine sulfate or p-sulfophenylalanine instead of glycine, showed enhanced gastric HCl secretion stimulation, compared to pentagastrin, but showed no anticonvulsant activity. Substitution of the N-terminal glycine with iminodiacetic acid, in pentagastrin, suppressed the gastrin-like activity, but enhanced the anticonvulsant activity.
IT **25126-32-3D**, CCK-8, analogs **102986-05-0**
RL: BIOL (Biological study)
(anticonvulsant and cholecystokinin and gastrin activity of)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



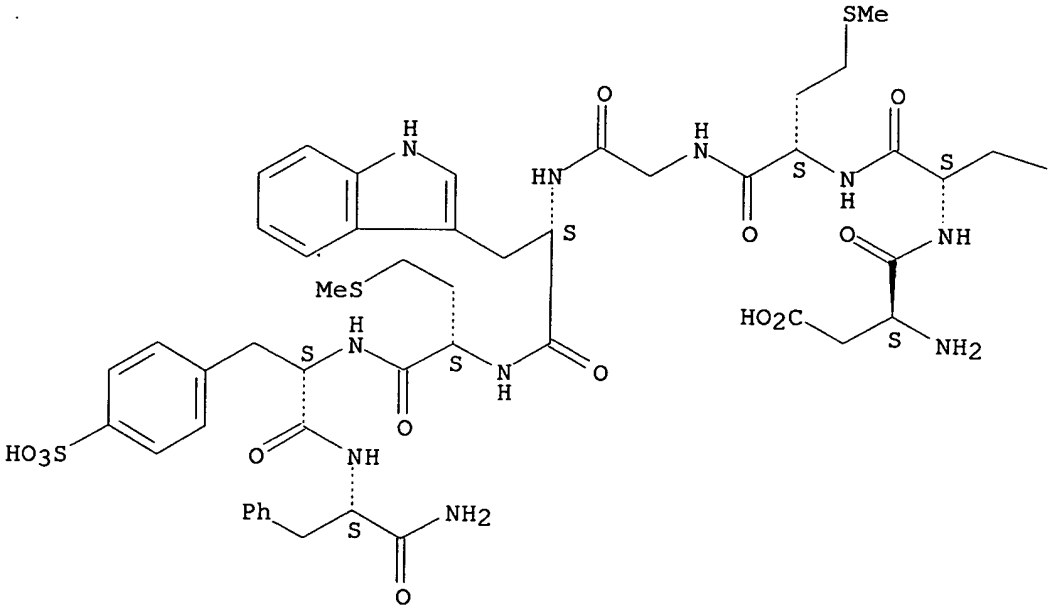
PAGE 1-B

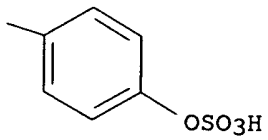
—OSO3H

RN 102986-05-0 CAPLUS
CN Caerulein, 1-de(5-oxo-L-proline)-2-de-L-glutamine-5-L-methionine-9-(4-sulfo-L-phenylalanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



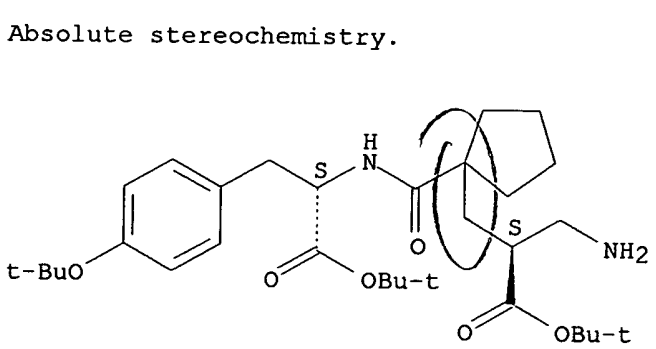

OSO3H

L24 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1992:129608 CAPLUS
DN 116:129608
TI Preparation of glutaryltyrosine cycloalkane derivatives as antihypertensives
IN Danilewicz, John Christopher; James, Keith; Collis, Alan John; Brown, David
PA Pfizer Ltd., UK; Pfizer Inc.
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9113054	A1	19910905	WO 1991-EP296	19910214
	W: CA, FI, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2073450	AA	19910827	CA 1991-2073450	19910214
	JP 05504146	T2	19930701	JP 1991-503973	19910214
	EP 594588	A1	19940504	EP 1991-903839	19910214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FI 9203780	A	19920821	FI 1992-3780	19920821
PRAI	GB 1990-4260		19900226		
	WO 1991-EP296		19910214		

OS MARPAT 116:129608
AB Title compds. I [A completes a 5- or 6-membered (monounsatd.) carbocyclic ring; Y = C1-9 alkylene; R1 = H, C1-4 alkyl; R, R4 = H, C1-6 alkyl, C3-7 cycloalkyl, benzyl, etc.; R2 = OH, (substituted) C1-6 alkoxy, C1-6 alkyl S(O)n, (substituted) amino, etc.; R3 = (substituted) CH2Ph, (substituted) 3-indolylmethyl, (substituted) 3-indazolylmethyl; n = 0-2] were prepd. as drugs for the treatment of a variety of conditions, e.g., hypertension (no data). Thus, 1-(2-tert-butoxycarbonyl-3-dibenzylaminopropyl)-1-cyclopentonecarboxylic acid was condensed with H-Tyr(CMe3)-OCMe3 in the presence of HOBT and EtN:C:N(CH2)3NMe2 and the resulting product was debenzylated. The product was then coupled with 4-tert-butoxycarbonylaminomethylbenzoic acid, followed by HCl hydrolysis to give title compd. II.
IT **129980-28-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate and/or drug)
RN 129980-28-5 CAPLUS
CN L-Tyrosine, N-[[1-[2-(aminomethyl)-3-(1,1-dimethylethoxy)-3-oxopropyl]cyclopentyl]carbonyl]-O-(1,1-dimethylethyl)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1989:74915 CAPLUS
DN 110:74915
TI Preparation of spiro-substituted glutaramides as diuretic agents
IN Barnish, Ian Thompson; James, Keith; Terrett, Nicholas Kenneth; Danilewicz, John Christopher; Samuels, Gillian Mary Ryder; Wythes, Martin James
PA Pfizer Ltd., UK
SO Eur. Pat. Appl., 119 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

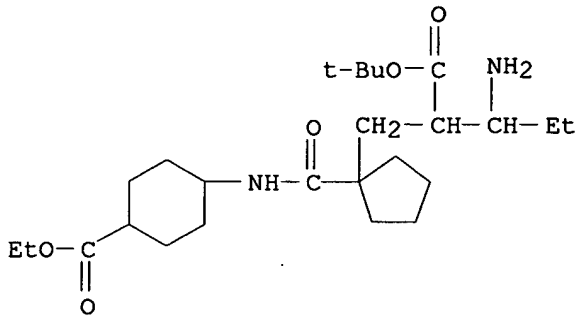
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 274234	A2	19880713	EP 1987-310784	19871208
	EP 274234	A3	19881019		
	EP 274234	B1	19910911		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 67178	E	19910915	AT 1987-310784	19871208
	IL 84757	A1	19920216	IL 1987-84757	19871208
	ES 2031523	T3	19921216	ES 1987-310784	19871208
	FI 8705413	A	19880612	FI 1987-5413	19871209
	FI 94336	B	19950515		
	FI 94336	C	19950825		
	ZA 8709247	A	19890726	ZA 1987-9247	19871209
	CA 1328264	A1	19940405	CA 1987-553863	19871209
	AU 8782407	A1	19880707	AU 1987-82407	19871210
	AU 595082	B2	19900322		
	HU 45487	A2	19880728	HU 1987-5576	19871210
	HU 202482	B	19910328		
	DK 8706484	A	19880819	DK 1987-6484	19871210
	DD 273831	A1	19891129	DD 1987-310250	19871210
	PL 150420	B1	19900531	PL 1987-269336	19871210
	SU 1612996	A3	19901207	SU 1987-4203861	19871210
	NO 174385	B	19940117	NO 1987-5169	19871210
	NO 174385	C	19940427		
	CN 87107371	A	19880706	CN 1987-107371	19871211
	CN 1016778	B	19920527		
	JP 63165353	A2	19880708	JP 1987-313951	19871211
	JP 05041627	B4	19930624		
PRAI	GB 1986-29663		19861211		
	GB 1987-15722		19870703		
	EP 1987-310784		19871208		

OS MARPAT 110:74915
AB The title compds. [I; X = Q; A = atoms to complete a 4- to 7-membered carbocycle which may be (mono-un)satd. or optionally fused to an (un)satd. 5- or 6-membered carbocycle; B = (CH2)m; m = 1-3; R, R4 = H, C1-6 alkyl, PhCH2, biolabile ester-forming group; R1 = H, C1-4 alkyl; R2, R3 = H, OH, C1-4 alkyl, C1-4 alkoxy; R5 = (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, aryl-C2-6 alkynyl), C3-7 cycloalkyl, C3-7 cycloalkenyl, C1-6 alkoxy, (un)substituted NH2, NR6COR7, NR6SO2R7, satd. heterocyclyl; R6 = H, C1-4 alkyl; R7 = C1-4 alkyl, CF3, aryl, heterocyclyl, C1-4 alkoxy, aryl(C1-4 alkyl), aryl(C1-4 alkoxy), (un)substituted NH2] (II), useful as diuretics (no data), were prepd. Ethyl[3-(dimethylamino)propyl]carbodiimide-HCl (6 mmol) was added to an ice-cold stirred mixt. of benzyl 3-(1-carboxycyclopentyl)-2-(2-methoxyethyl)propanoate (prepn. given), benzyl cis-4-aminocyclohexanecarboxylate tosylate, 1-hydroxybenzotriazole,

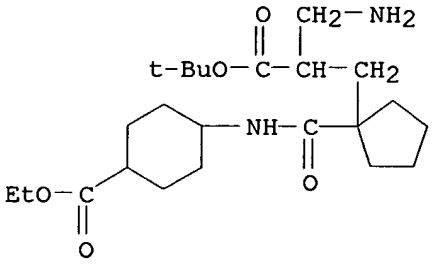
and N-methylmorpholine in dry CH2Cl2. The mixt. was warmed to room temp. and stirred for 18 h to give 67% benzyl 3-[1-[[cis-4-(benzyloxycarbonyl)cyclohexyl]carbamoyl]cyclopentyl]-2-(2-methoxyethyl)propanoate.

IT **118755-03-6P 118755-04-7P 118755-05-8P 118784-42-2P 118785-37-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as diuretic)

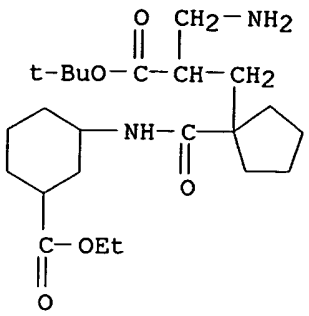
RN 118755-03-6 CAPLUS
CN Cyclohexanecarboxylic acid, 4-[[[1-[3-amino-2-[(1,1-dimethylethoxy)carbonyl]pentyl]cyclopentyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



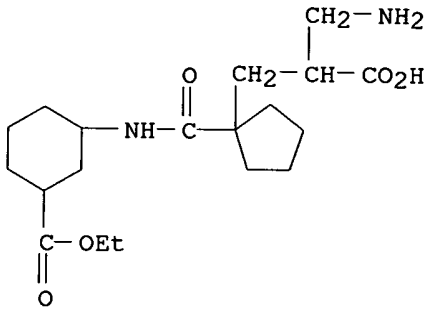
RN 118755-04-7 CAPLUS
CN Cyclohexanecarboxylic acid, 4-[[[1-[2-(aminomethyl)-3-(1,1-dimethylethoxy)-3-oxopropyl]cyclopentyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



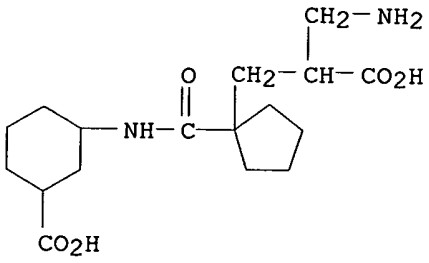
RN 118755-05-8 CAPLUS
CN Cyclohexanecarboxylic acid, 3-[[[1-[2-(aminomethyl)-3-(1,1-dimethylethoxy)-3-oxopropyl]cyclopentyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



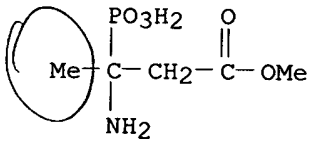
RN 118784-42-2 CAPLUS
CN Cyclohexanecarboxylic acid, 3-[[[1-(3-amino-2-carboxypropyl)cyclopentyl]carbonyl]amino]-, 1-ethyl ester (9CI) (CA INDEX NAME)



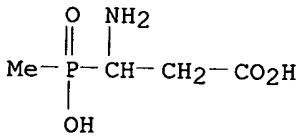
RN 118785-37-8 CAPLUS
CN Cyclohexanecarboxylic acid, 3-[[[1-(3-amino-2-carboxypropyl)cyclopentyl]carbonyl]amino]- (9CI) (CA INDEX NAME)



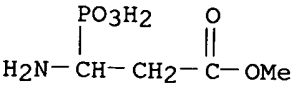
L24 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1987:451405 CAPLUS
DN 107:51405
TI Preliminary pharmacological evaluation of newly synthesized derivatives of phosphonoamino acids
AU Kleinrok, Zdzislaw; Kolasa, Krystyna; Mastalerz, Przemyslaw; Kafarski, Pawel
CS Dep. Pharmacol., Med. Acad., Lublin, 20-090, Pol.
SO Polish Journal of Pharmacology and Pharmacy (1986), 38(5-6), 435-42
CODEN: PJPPAA; ISSN: 0301-0244
DT Journal
LA English
AB Ten newly synthesized derivs. of phosphonoamino acids were subjected to preliminary pharmacol. evaluation in mice and rats. Their effect on acute toxicity, body temp., spontaneous and exploratory activity, electrogenic and pentetrazole convulsions, and motor coordination and .gamma.-amino-butyric acid concn. in various brain regions was investigated. The most active derivs. were .alpha.-amino-.alpha.-p-hydroxyphenylmethylphosphonic acid, .beta.-(.alpha.-aminoethyl)-carbamoylethylphosphonic acid, .alpha.-amino-.beta.-phenylethylphosphonic acid, and .alpha.-amino-.beta.-(p-nitrophenyl)ethylphosphonic acid. Those compds. depressed the spontaneous locomotor activity and displayed protective action in electrogenic and pentetrazole convulsions.
IT **81746-53-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of)
RN 81746-53-4 CAPLUS
CN Butanoic acid, 3-amino-3-phosphono-, 1-methyl ester (9CI) (CA INDEX NAME)



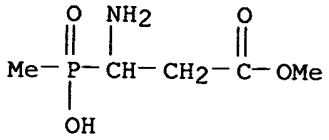
L24 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1986:218953 CAPLUS
DN 104:218953
TI Preliminary pharmacological investigation on 38 aminophosphonic acids and their derivatives
AU Kleinrok, Zdzislaw; Kolasa, Krystyna; Chodkowska, Anna; Mastalerz, Przemyslaw; Kafarski, Pawel
CS Inst. Clin. Pathol., Med. Acad., Lublin, 20-090, Pol.
SO Polish Journal of Pharmacology and Pharmacy (1985), 37(5), 575-84
CODEN: PJPPAA; ISSN: 0301-0244
DT Journal
LA English
AB Central pharmacol. properties of 38 aminophosphonic acids and their derivs., were investigated on mice and rats. Acute toxicity, neurotoxic activity and the influence on spontaneous locomotor activity, body temp., electrogenic and pentetrazol convulsions and on the cerebral GABA [56-12-2] level were tested. The most active anticonvulsant compds. were (in a decreasing order of activity): 2-amino-7-phosphonoheptanoic acid [85797-13-3], 2-amino-5-phosphonovaleric acid [76726-92-6], 2-amino-8-phosphonooctanoic acid [98517-63-6], 2-amino-2-methyl-3-methylphosphonopropionic acid [73870-67-4], and 3-amino-3-hydroxy-5-phosphonovaleric acid acid [99305-89-2]. Some structure-activity relations are discussed.
IT **61341-13-7 61341-15-9 61341-16-0**
73870-70-9 73870-71-0 102394-10-5
RL: BIOL (Biological study)
(central pharmacol. properties of)
RN 61341-13-7 CAPLUS
CN Propanoic acid, 3-amino-3-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



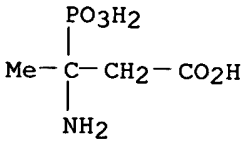
RN 61341-15-9 CAPLUS
CN Propanoic acid, 3-amino-3-phosphono-, 1-methyl ester (9CI) (CA INDEX NAME)



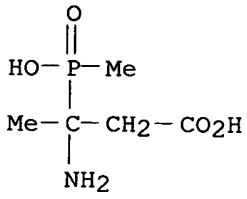
RN 61341-16-0 CAPLUS
CN Propanoic acid, 3-amino-3-(hydroxymethylphosphinyl)-, methyl ester (9CI) (CA INDEX NAME)



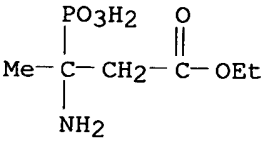
RN 73870-70-9 CAPLUS
CN Butanoic acid, 3-amino-3-phosphono- (9CI) (CA INDEX NAME)



RN 73870-71-0 CAPLUS
CN Butanoic acid, 3-amino-3-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



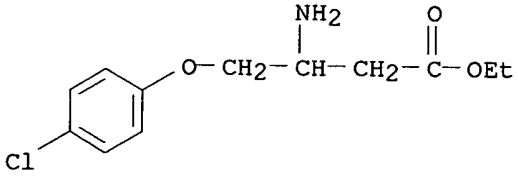
RN 102394-10-5 CAPLUS
CN Butanoic acid, 3-amino-3-phosphono-, 1-ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1985:504988 CAPLUS
DN 103:104988
TI Perhydro-1,3-oxazin-2-ones
IN Bourgery, Guy; Bucher, Bernard; Guerret, Patrick; Mocquet, Gisele; Moinet, Gerard
PA Delalande S. A. , Fr.
SO Fr. Demande, 30 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

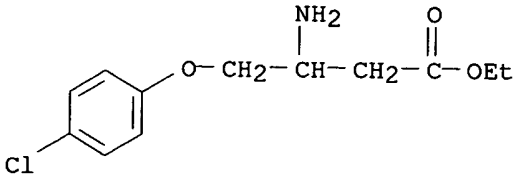
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2545488	A1	19841109	FR 1983-7270	19830502
	FR 2545488	B1	19851220		
PRAI	FR 1983-7270		19830502		

OS CASREACT 103:104988
AB Title compds. I [R = Ph, halo-, alkyl-, alkoxy-, nitro-, cyano-, or (trifluoromethyl)phenyl; R1 = H, alkyl; (n,m,p) = (1,1,1), (1,0,2), (0,0,2), (1,0,1)] were prepd. and they exhibited anticonvulsant activity. Thus, 4-ClC6H4OCH2CH(CH2NHCO2Et)CH2OH was heated with NaOMe in MeOH to give I (n = m = p = 1, R = 4-ClC6H4, R1 = H).
IT **97900-74-8P 97900-75-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 97900-74-8 CAPLUS
CN Butanoic acid, 3-amino-4-(4-chlorophenoxy)-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

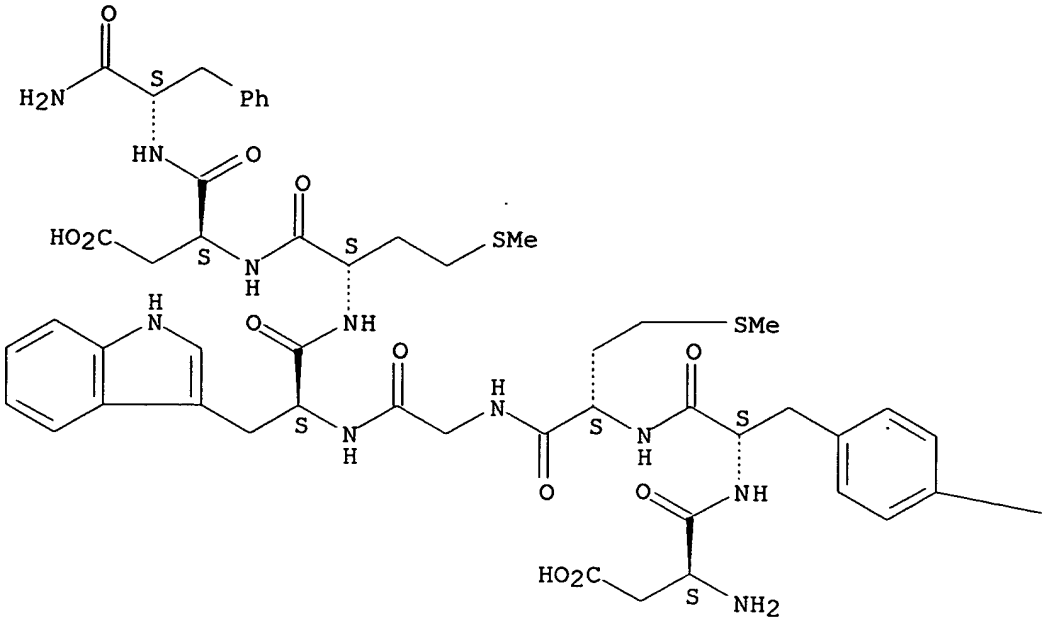
RN 97900-75-9 CAPLUS
CN Butanoic acid, 3-amino-4-(4-chlorophenoxy)-, ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1985:179251 CAPLUS
DN 102:179251
TI Effects of cholecystokinin octapeptides and their fragments on seizures induced by different convulsive drugs
AU Kadar, T.; Pesti, A.; Toth, G.; Penke, B.; Telegdy, G.
CS Dep. Pathophysiol., Univ. Med. Sch., Szeged, Hung.
SO Neuropept. Psychosom. Processes, Int. Conf. Integr. Neurohumoral Mech. (1983), Meeting Date 1982, 231-8. Editor(s): Endroczi, Elember. Publisher: Akad. Kiado, Budapest, Hung.
CODEN: 53HNAO
DT Conference
LA English
AB The antagonist activities of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [**25126-32-3**], nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**] and fragments of these mols. on convulsive seizures induced by pentetrazole [54-95-5], strychnine [57-24-9], and picrotoxin [124-87-8] were examd. in mice and rats. Peptides were administered i.p. to mice and intracerebroventricularly to rats, 10 min before administration of the convulsant drug. CCK-8-SE and CCK-8-NS antagonized picrotoxin-induced seizures in both mice and rats, but had no effect on strychnine and pentetrazole-induced convulsions. In both species the octapeptide fragments which attenuated picrotoxin-induced seizures or prolonged the time until death contained the C-terminal tetrapeptide amide (CCK-5-8 [1947-37-1]) sequence of the mol. The C-terminal tripeptide (CCK-6-8 [5934-92-9]) and dipeptide (CCK-7-8 [5241-71-4]) had no anticonvulsive activity. The N-terminal nonsulfated tetrapeptide (CCK-1-4-NS [**80790-40-5**]) also slightly antagonized the effect of picrotoxin, but only in rats.
IT **25126-32-3 25679-24-7 80790-40-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

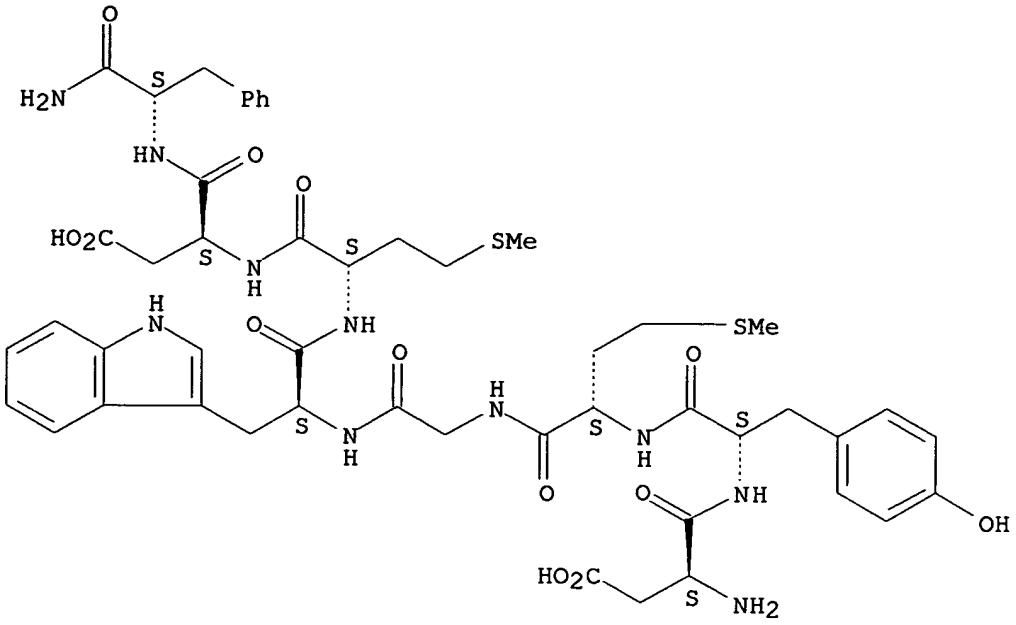


PAGE 1-B

—OSO3H

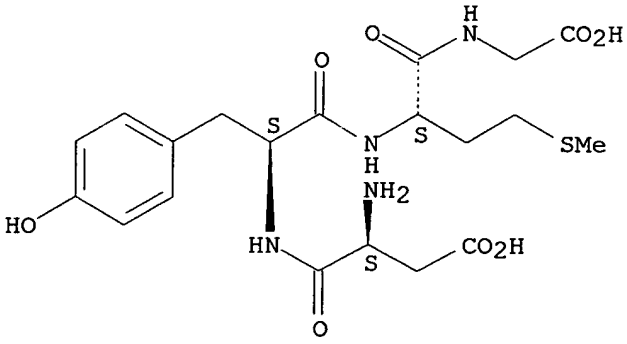
RN 25679-24-7 CAPLUS
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

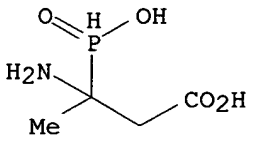


RN 80790-40-5 CAPLUS
CN Glycine, L-.alpha.-aspartyl-L-tyrosyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



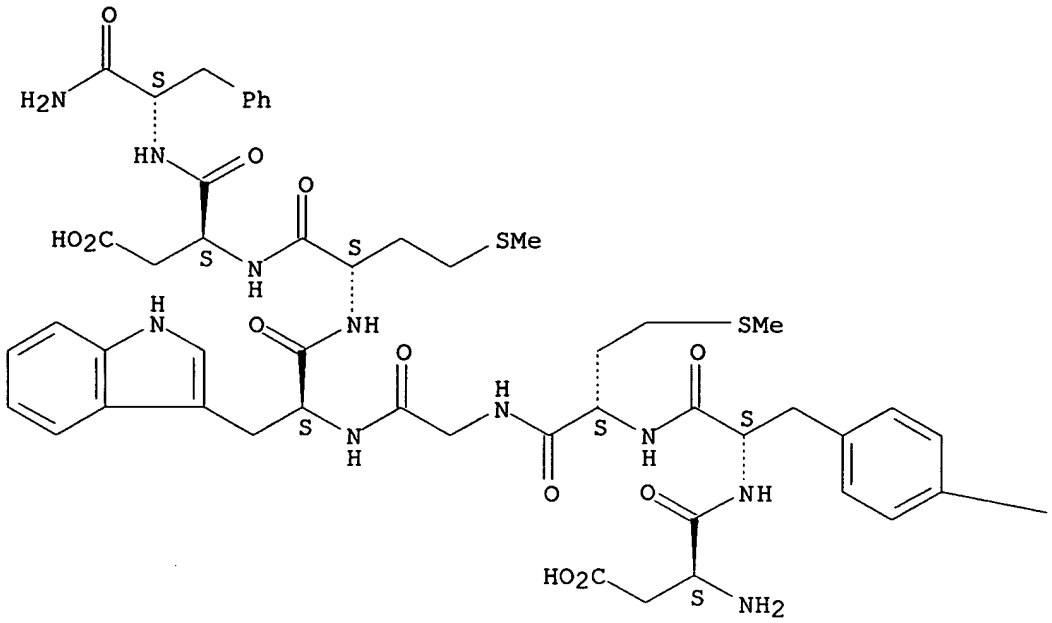
L24 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1985:78999 CAPLUS
DN 102:78999
TI Excitatory amino acid receptor interactions of a novel .alpha.-phosphinic acid analog of .alpha.-methylaspartic acid
AU Cates, L. A.; Li, V. S.; Hu, Z. S.; Lehmann, J.; Coyle, J. T.; Ferkany, J. W.
CS Coll. Pharm., Univ. Houston, Houston, TX, 77004, USA
SO Journal of Pharmaceutical Sciences (1984), 73(11), 1550-3
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB Reaction of Ph2CHNH2, AcCH2CO2Et, and H3PO2 gave Ph2CHNHCMe(CH2CO2Et)P(O)(H)(OH), which was sapond., then cleaved to give the P analog, H2NCMe(CH2CO2H)P(O)(H)(OH) (I). I did not interact with excitatory amino acid receptors directly, as assessed by direct in vitro radioreceptor binding methods. However, I has a weak anticonvulsant activity and exhibits an excitant action in vitro that is apparently not mediated by a N-methyl-D-aspartate receptor.
IT **94650-45-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and biol. activity of)
RN 94650-45-0 CAPLUS
CN Butanoic acid, 3-amino-3-(hydroxyphosphinyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1984:564133 CAPLUS
DN 101:164133
TI Inhibition of seizures induced by picrotoxin and electroshock by cholecystokinin octapeptides and their fragments in rats after intracerebroventricular administration
AU Kadar, T.; Pesti, A.; Penke, B.; Telegdy, G.
CS Univ. Med. Sch., Inst. Pathophysiol., Szeged, H-6701, Hung.
SO Neuropharmacology (1984), 23(8), 955-61
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB The anticonvulsive activity of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [**25126-32-3**], nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**], and 3 different N- and C-terminal fragments were investigated against seizures induced by picrotoxin [124-87-8] and electroshock in rats after intracerebroventricular administration. Doses of 0.8 and 80 pmol of CCK-8-SE and CCK-8-NS enhanced the latency of seizures induced by picrotoxin and shortened the duration of the clonic phase of the seizures induced by electroshock. Only CCK-8-SE shortened the recovery time and only 0.8 pmol of CCK-8-SE shortened the duration of the tonic phase of convulsions induced by electroshock. Doses of the octapeptides of 8000 pmol were ineffective, with the exception of CCK-8-NS in the picrotoxin test. Of the fragments tested, the C-terminal tetrapeptide (CCK-5-8) [1947-37-1] enhanced the latency of seizures induced by picrotoxin in a dose of 0.8 pmol, and had a dose-dependent biphasic effect on the duration of the clonic phase of seizures induced by electroshock. Intracerebroventricular administration of diazepam [439-14-5] enhanced only the latency of tremor and clonic seizures induced with picrotoxin in a dose of 40 nmol. Twelve nmole of diazepam shortened the clonic phase of convulsions induced by electroshock. The peptides tested were much more active than diazepam, and their EDs were comparable to the amts. of cholecystokinin octapeptide found in brain structures.
IT **25126-32-3 25126-32-3D**, fragments **92510-63-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, after brain administration)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



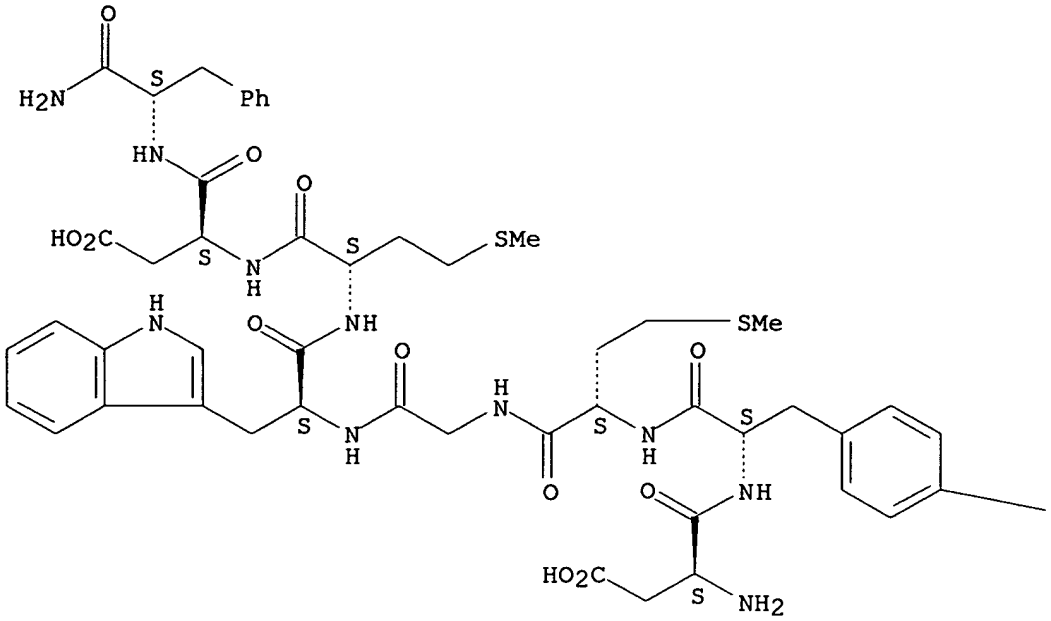
PAGE 1-B

—OSO3H

RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

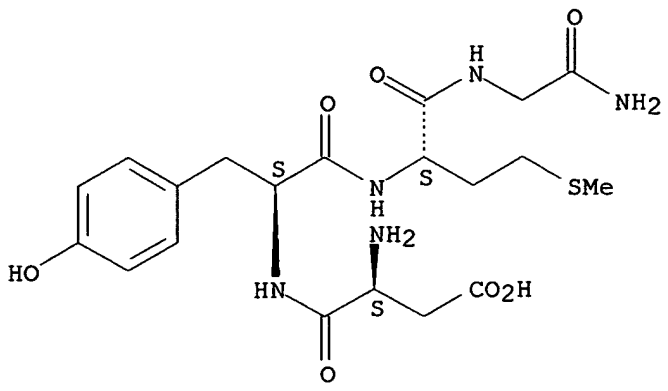


PAGE 1-B

—OSO3H

RN 92510-63-9 CAPLUS
CN Glycinamide, L-.alpha.-aspartyl-L-tyrosyl-L-methionyl- (9CI) (CA INDEX NAME)

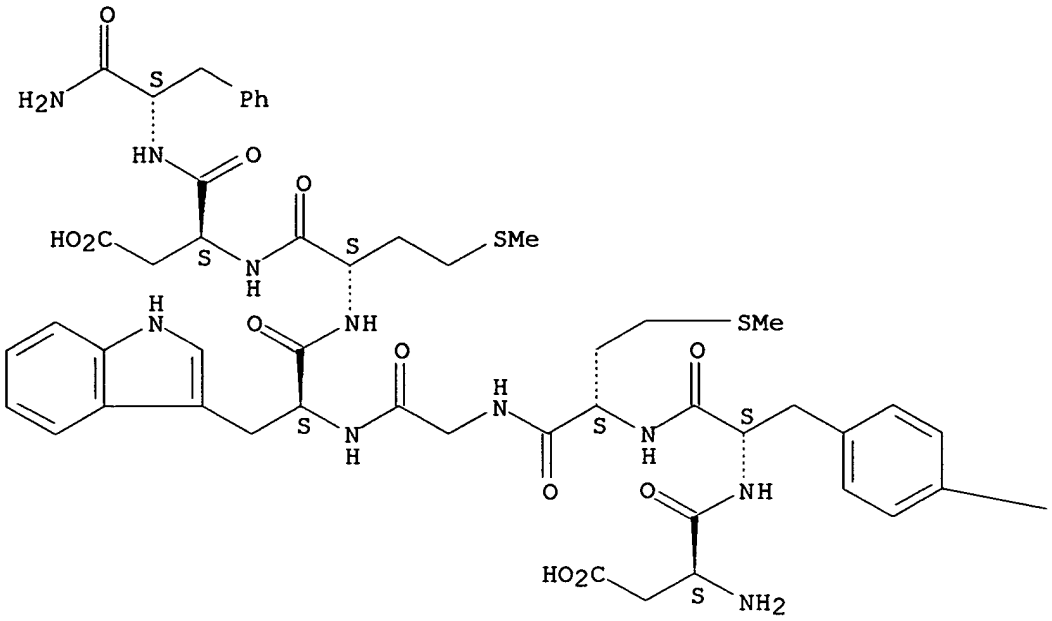
Absolute stereochemistry.



L24 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1984:45457 CAPLUS
DN 100:45457
TI Structure-activity and dose-effect relationships of the antagonism of picrotoxin-induced seizures by cholecystokinin, fragments and analogs of cholecystokinin in mice
AU Kadar, T.; Pesti, A.; Penke, B.; Toth, G.; Zarandi, M.; Telegdy, G.
CS Dep. Pathophysiol., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Neuropharmacology (1983), 22(10), 1223-9
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB I.p. administration of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [**25126-32-3**] and nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**] enhanced the latency of seizures induced by picrotoxin in mice. Expts. with N- and C-terminal fragments revealed that the C-terminal tetrapeptide (CCK-5-8) [1947-37-1] was the active center of the CCK octapeptide mol. The analogs CCK-8-SE and CCK-8-NS (0.2-6.4 .mu.mol/kg) and caerulein (0.1-0.8 .mu.mol/kg) showed bell-shaped dose-effect curves, with the greatest max. inhibition for CCK-8-NS. CCK-5-8 had weak anticonvulsant activity in comparison to the octapeptides; 3.2 .mu.mol/kg and larger doses of the ref. drug, diazepam, totally prevented picrotoxin-induced seizures and mortality. The max. effect of the peptides tested was less than that of diazepam. Expts. with analogs and derivs. of CCK-5-8 demonstrated that the effectiveness of the .beta.-alanyl derivs. of CCK-5-8 were enhanced and that they were equipotent with CCK-8-SE. Of the CCK-2-8 analogs, Ser(SO3H)7-Ac-CCK-2-8-SE [88457-86-7], Thr(SO3H)7-Ac-CCK-2-8-SE [88457-87-8], and Hyp(SO3H)-Ac-CCK-2-8-SE [88457-88-9] were slightly more active than CCK-8-SE.
IT **25126-32-3 25679-24-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anticonvulsant action of, mol. structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

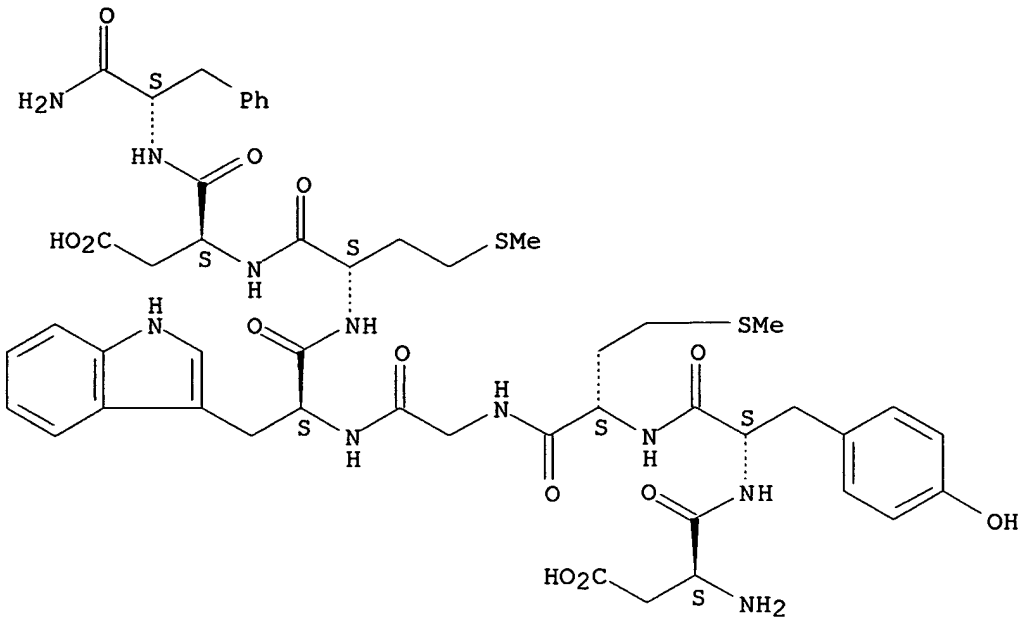


PAGE 1-B

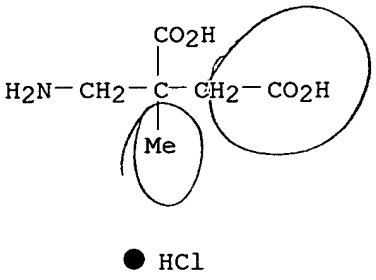
—OSO3H

RN 25679-24-7 CAPLUS
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



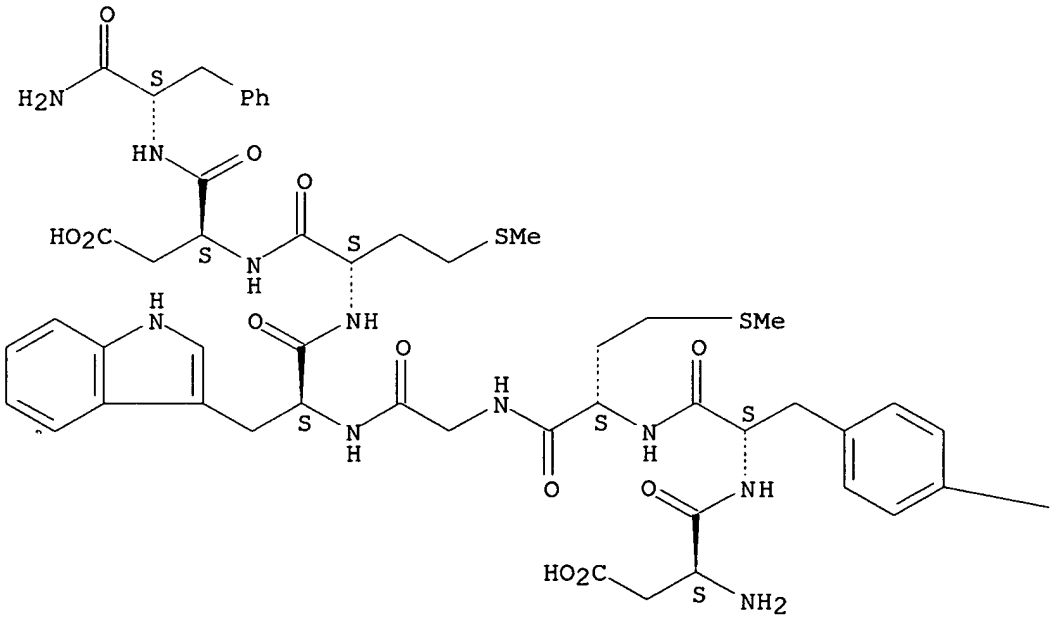
L24 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1983:539853 CAPLUS
DN 99:139853
TI Synthesis of aminomethyl-substituted cyclic imide derivatives for evaluation as anticonvulsants
AU Stratford, Eugene S.; Curley, Robert W., Jr.
CS Sch. Pharm., Univ. West Virginia, Morgantown, WV, 26506, USA
SO Journal of Medicinal Chemistry (1983), 26(10), 1463-9
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 99:139853
AB A series of aminomethyl-substituted cyclic imides based on the 2,5-pyrrolidinedione and 2,4-imidazolidinedione ring systems has been prepd. The 3-(aminomethyl)-2,5-pyrrolidinediones were prepd. by a dehydration procedure beginning with N-benzyl-2-(aminomethyl)succinic acid, whereas the 3-aminomethyl)-3-methyl-2,3-pyrrolidinediones were best obtained by fusion of the amine salts of 2-(aminomethyl)-2-methylsuccinic acid. The hydantoin deriv. I was obtained by std. procedures. Although none of the compds. tested showed significant activity against convulsions induced by pentylenetetrazole (PTZ), some showed significant activity against maximal electroshock seizures in mice.
IT **86970-16-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amination of)
RN 86970-16-3 CAPLUS
CN Butanedioic acid, 2-(aminomethyl)-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



L24 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1982:538831 CAPLUS
DN 97:138831
TI Ceruletide, ceruletide analogs and cholecystokinin octapeptide (CCK-8): effects of motor behavior, hexobarbital-induced sleep and harman-induced convulsions
AU Zetler, G.
CS Inst. Pharmakol., Med. Hochsch. Luebeck, Luebeck, D-2400, Fed. Rep. Ger.
SO Peptides (New York, NY, United States) (1982), 3(4), 701-4
CODEN: PPTDD5; ISSN: 0196-9781
DT Journal
LA English
AB The effects of s.c. administration of 10 ceruletide analogs, cholecystokinin octapeptide **[25126-32-3]**, and ceruletide [17650-98-5] on the prodn. of catalepsy, prolongation of hexobarbital-induced sleep, and delay in onset of harman-induced convulsions were studied in mice. Ceruletide and several analogs were more potent than the ref. drugs, diazepam and haloperidol. Desulfation, deamidation, and shortening of the peptide chain by 5 amino acids strongly reduced or abolished the pharmacol. activities of ceruletide. Other chem. modifications weakened the efficacy to an unequal extent for the 3 effects and altered the pharmacol. selectivity.
IT **25126-32-3**
RL: BIOL (Biological study)
(behavior response to, structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

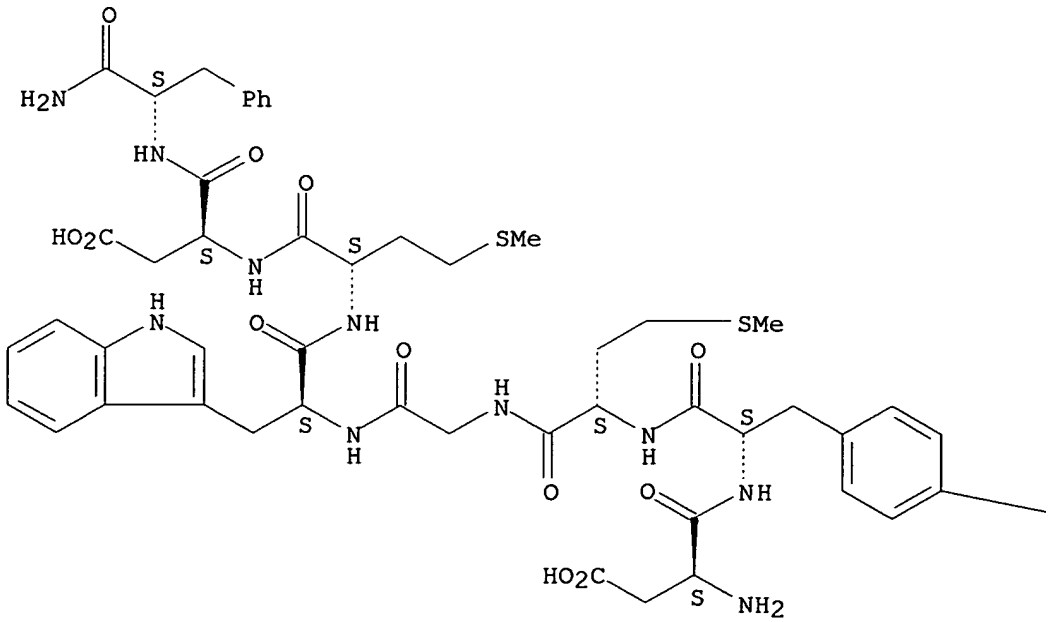


—OSO_3H

L24 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1982:155725 CAPLUS
DN 96:155725
TI Central effects of ceruletide analogs
AU Zetler, G.
CS Inst. Pharmakol., Med. Hochsch. Luebeck, Luebeck, D-2400, Fed. Rep. Ger.
SO Peptides (New York, NY, United States) (1982), Volume Date 1981, 2(Suppl. 2, Brain-Gut Axis: New Front.), 65-9
CODEN: PPTDD5; ISSN: 0196-9781
DT Journal
LA English
AB Ten ceruletide [17650-98-5] analogs and cholecystokinin octapeptide [**25126-32-3**] were compared with ceruletide regarding neuropharmacol. effects in mice after peripheral administration. The effects under study were inhibition of motor response to noxious stimulation (hot plate), prodn. of ptosis, inhibition of exploratory rearing activity, elevation of threshold for picrotoxin-induced convulsions, and antagonism of methylphenidate-induced gnawing. Desulfation, deamidation, and shortening of the peptide chain by 5 amino acids destroyed all pharmacol. activities of ceruletide. Other modifications were of unequal consequences for the pharmacol. profile of a given analog, decreasing some effects while increasing others. Hence, structural changes of the ceruletide mol. resulted in modulations of both potency and selectivity.
IT **25126-32-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neuropharmacol. activity of, structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

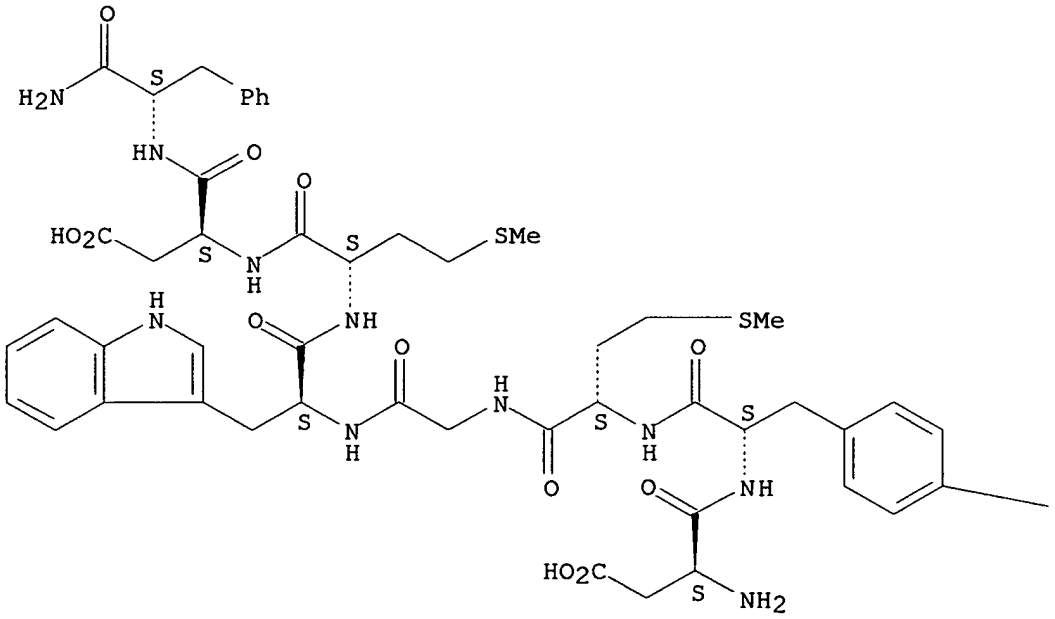


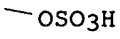
—OSO_3H

L24 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1980:561255 CAPLUS
DN 93:161255
TI Anticonvulsant effects of caerulein and cholecystokinin octapeptide, compared with those of diazepam
AU Zetler, Gerhard
CS Inst. Pharmakol., Med. Hochsch. Luebeck, Luebeck, D-2400, Fed. Rep. Ger.
SO European Journal of Pharmacology (1980), 65(2-3), 297-300
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB Caerulein [17650-98-5] and the C-terminal octapeptide of cholecystokinin (CCK-8) [**25126-32-3**], after s.c. administration to mice, delayed the onset and retarded the development of toxic effects of convulsants such as strychnine, pentetrazol, bicuculline, and picrotoxin. They also increased the seizure threshold doses of i.v. infused pentetrazol and picrotoxin. In this regard, both peptides were at least equipotent with diazepam.
IT **25126-32-3**
RL: PRP (Properties)
(anticonvulsant effects of)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



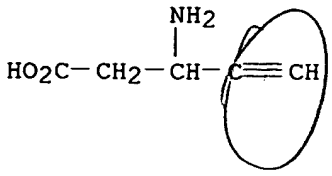


L24 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1976:542651 CAPLUS
DN 85:142651
TI Acetylene derivatives of amino acids
IN Metcalf, Brian W.; Jung, Michel
PA Richardson-Merrell Inc., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3959356	A	19760525	US 1975-559547	19750318
	NO 7600235	A	19760921	NO 1976-235	19760126
	NO 147104	B	19821025		
	NO 147104	C	19830202		
	ZA 7600410	A	19770126	ZA 1976-410	19760126
	GB 1467138	A	19770316	GB 1976-2855	19760126
	DK 7600313	A	19760919	DK 1976-313	19760127
	DK 147126	B	19840416		
	DK 147126	C	19840924		
	IL 48911	A1	19800731	IL 1976-48911	19760127
	AU 7610713	A1	19770811	AU 1976-10713	19760202
	SE 7601207	A	19760919	SE 1976-1207	19760204
	SE 427029	B	19830228		
	SE 427029	C	19830609		
	NL 7601117	A	19760921	NL 1976-1117	19760204
	JP 51125319	A2	19761101	JP 1976-16076	19760218
	CA 1080715	A1	19800701	CA 1976-246111	19760219
	CH 630604	A	19820630	CH 1976-2205	19760223
	DE 2607592	A1	19760930	DE 1976-2607592	19760225
	ES 445660	A1	19771001	ES 1976-445660	19760228
	US 4041041	A	19770809	US 1976-664516	19760308
	FR 2304330	A1	19761015	FR 1976-7549	19760316
	FR 2304330	B1	19800718		
	BE 839658	A1	19760716	BE 1976-165246	19760317
	CA 1088562	A2	19801028	CA 1979-340370	19791122
PRAI	US 1975-559547		19750318		
	CA 1976-246111		19760219		

AB Amino acids CH.tplbond.CCH(NH2)ZCO2H [Z = (CH2)2 (I), CH2, (CH2)3, CHPhCH2, CH:CH] and I amides and esters, useful as sedatives, .gamma.-aminobutyric acid transaminase inhibitors, antiobesity agents, and in the treatment of central nervous system disorders, were prepd. Thus, Me3SiC.tplbond.CCH2N:CHPh, prepd. from CH.tplbond.CCH2NH2 in 2 steps, was treated with BuLi and CH2:CHCO2Me in THF and the product was heated with aq. HCl at reflux to give I, which was resolved into (+)-I and (-)-I via (+)-binaphthylphosphoric acid salts. I at a dose of 100-200 mg/kg in mice and rats decreased the motor activity, which was still observable 48 hr after administration; I at a dose of 50-200 mg/kg in mice gave complete protection against audiogenic seizures lasting for over 16 hr.

IT **60625-83-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for use as pharmacological agent)
RN 60625-83-4 CAPLUS
CN 4-Pentynoic acid, 3-amino- (9CI) (CA INDEX NAME)



```
=> s convulsiv? or anticonvulsiv?
          3622 CONVULSIV?
          1662 ANTICONVULSIV?
L25       5142 CONVULSIV? OR ANTICONVULSIV?

=> s l18 and l25
         28144 L18
L26         10 L18 AND L25

=> s l26 not l21
L27          8 L26 NOT L21

=> d l27 1-8 bib,ab,hitstr
```

L27 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:381826 CAPLUS
DN 136:350580
TI Method for treating glioma aggravated with epileptic syndrome
IN Korytova, L. I.; Zhabina, R. M.; Sokurenko, V. P.; Vartanyan, L. P.
PA Tsentral'nyi Nauchno-Issledovatel'skii Rentgenoradiologicheskii Institut, Russia
SO Russ., No pp. given
CODEN: RUXXE7
DT Patent
LA Russian
FAN.CNT 1

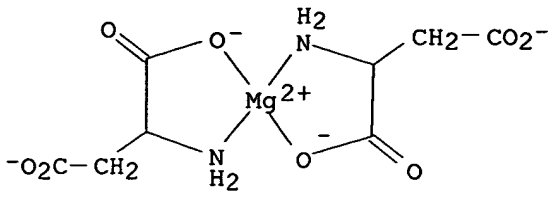
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI RU 2166948	C1	20010520	RU 2000-113130	20000529
PRAI RU 2000-113130		20000529		

AB The proposed method involves per os administration of riboxin to a patient, after surgical removal of the tumor, at a dose of 0.2 g, 3 times a day, for 5-10 days. Radiation therapy is started at the same time. I.v. (and later peroral) riboxin and proxiphein are administered. Riboxin is i.v. injected at a dose of 10 mL during the first two weeks and then per os at a dose of 0.2 g three times a day for up to 3 mo. Proxiphein is administered according to the following scheme: 2 days the dose is 0.25 g once a day, two days - 0.25 g twice a day, and then, the dose is 0.25 g three times a day during 40-45 days. The chemotherapy course is repeated 4-5 wk later. Benzonal is applied as an **anticonvulsive** prepn. at a dose of 0.1 g or finlepsin at a dose of 0.2 g 3 times a day during the first two weeks and then two times a day to the end of the chemotherapy course and later at a dose of 1 tablet before going to bed for not less than 2-3 yr. Enhanced effectiveness of the treatment was achieved by the proposed method.

IT **8076-65-1**, Panangin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of glioma aggravated with epileptic syndrome)
RN 8076-65-1 CAPLUS
CN Aspartic acid, monopotassium salt, mixt. with potassium hydrogen (T-4)-bis[aspartato(2-)-.kappa.N,.kappa.O1]magnesate(2-) (9CI) (CA INDEX NAME)

CM 1

CRN 32679-51-9
CMF C8 H10 Mg N2 O8 . H . K
CCI CCS

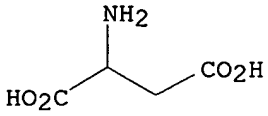


● H^+

● K^+

CM 2

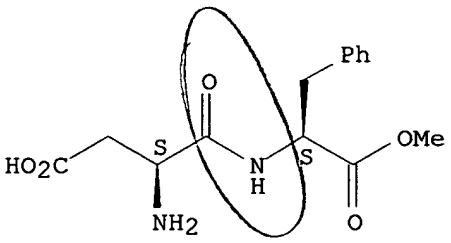
CRN 923-09-1
CMF C4 H7 N O4 . K



● K

L27 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1989:422331 CAPLUS
DN 111:22331
TI Aspartame fails to facilitate pentylenetetrazole-induced convulsions in CD-1 mice
AU Dailey, John W.; Lasley, Stephen M.; Mishra, Pravin K.; Bettendorf, Anne F.; Burger, Robert L.; Jobe, Phillip C.
CS Coll. Med., Univ. Illinois, Peoria, IL, 61656, USA
SO Toxicology and Applied Pharmacology (1989), 98(3), 475-86
CODEN: TXAPA9; ISSN: 0041-008X
DT Journal
LA English
AB Concns. of plasma amino acids and brain monoamines as well as pentylenetetrazole-induced seizures were monitored in CD-1 mice treated with aspartame in acute oral doses .ltoreq.2.5 g/kg. One h after administration aspartame produced increases in plasma concns. of phenylalanine and tyrosine and modest redns. in concns. of brain serotonin and 5-hydroxyindoleacetic acid. The sweetener had no influence on the median **convulsive** dose (CD50) of pentylenetetrazole; it failed to alter the percentage of mice exhibiting seizures when exposed to an approx. CD50 of pentylenetetrazole and had no effect on brain norepinephrine or dopamine concns. In contrast to previous reports these observations suggest that aspartame in high doses does not alter the propensity to seizure activity in CD-1 mice. Apparently, the changes in plasma amino acids and brain serotonin produced by large oral doses of aspartame are insufficient to result in functional deficits which might have the capacity to facilitate pentylenetetrazole-induced seizures.
IT **22839-47-0**, Aspartame
RL: BIOL (Biological study)
(convulsions in relation to dietary)
RN 22839-47-0 CAPLUS
CN L-Phenylalanine, L-.alpha.-aspartyl-, 2-methyl ester (9CI) (CA INDEX NAME)

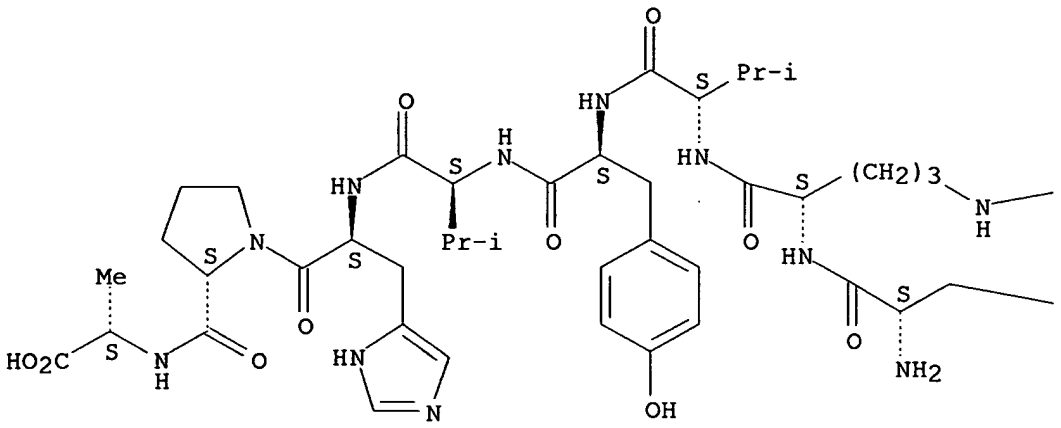
Absolute stereochemistry.



L27 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1986:565177 CAPLUS
DN 105:165177
TI Central effects of angiotensin II, its fragment and analogs
AU Georgiev, V.; Klusha, V.; Petkov, V.; Markovska, V.; Svirskis, S.; Munceniecse, R.; Anuans, Z.
CS Inst. Physiol., Sofia, Bulg.
SO Acta Physiologica et Pharmacologica Bulgarica (1984), 10(4), 36-43
CODEN: APPBDI; ISSN: 0323-9950
DT Journal
LA English
AB The effects of angiotensin II amide (AT II) [53-73-6], its fragment [Ile8]-AT3-8 [81417-71-2], and the analogs [Sar1,Ala8]-AT II [34273-10-4], [Ala8]-AT II [**38023-97-1**], and [Ile8]-AT II [**52670-43-6**] were studied with respect to the level of biogenic amines (dopamine (DA) [51-61-6] and 5-HT [50-67-9] and their resp. metabolites homovanillic acid (HVA) [306-08-1] and 5-HIAA [54-16-0]) in the forebrain and the behavior of the animals (haloperidol catalepsy, apomorphine stereotypy, unconditioned jumping reaction (UJR), and **convulsive** threshold). A good correlation was found between the biochem. and behavioral effects. The fragment of AT II where phenylalamine is substituted at the C-terminal by isoleucine reduced the haloperidol-increased content of HVA, potentiated apomorphine stereotypy, and reduced catalepsy, whereas the AT II analogs (where the C-terminal phenylalamine is substituted by alanine and the N-terminal by sarcosine) potentiated the effect of haloperidol increasing the HVA content, reduced apomorphine stereotypy, and potentiated catalepsy; saralasin independently applied induced brief catalepsy; AT II and its fragment and analog inhibited UJR, in combination with amphetamine and PTZ this effect became deeper; the duration of hexobarbital sleep was increased. The peptides investigated increased the **convulsive** threshold. Apparently, the hexapeptide fragment has preserved the effects of AT II, whereas in the analog (with changed C- and N-terminals) they are changed. The results obtained may be explained with the modulating influence of AT II-receptors on the dopaminergic receptors in the brain structures with which AT II and its fragment and analogs enter in contact.
IT **38023-97-1 52670-43-6**
RL: BIOL (Biological study)
(amines of brain and behavior response to, structure in relation to)
RN 38023-97-1 CAPLUS
CN L-Alanine, N-[1-[N-[N-[N-[N-(N2-L-.alpha.-aspartyl-L-arginyl)-L-valyl]-L-tyrosyl]-L-valyl]-L-histidyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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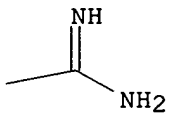
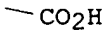
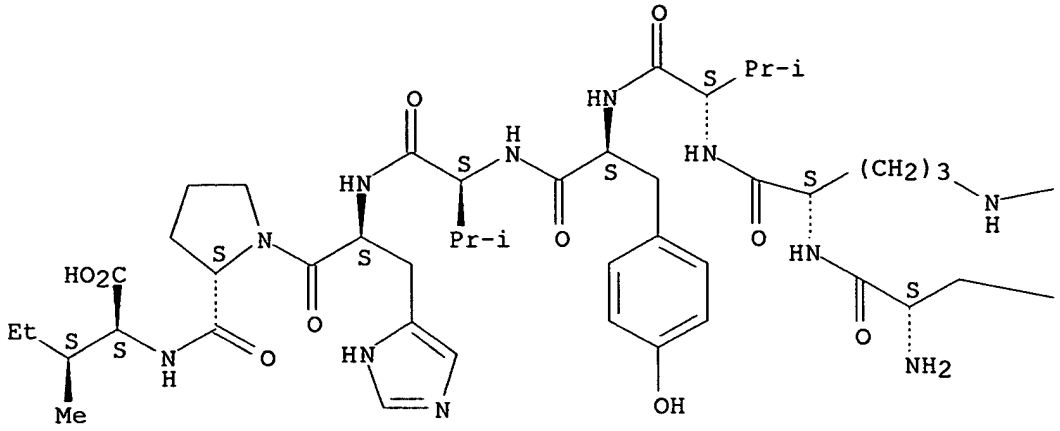




RN 52670-43-6 CAPLUS
CN Angiotensin II, 5-L-valine-8-L-isoleucine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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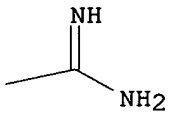
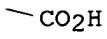
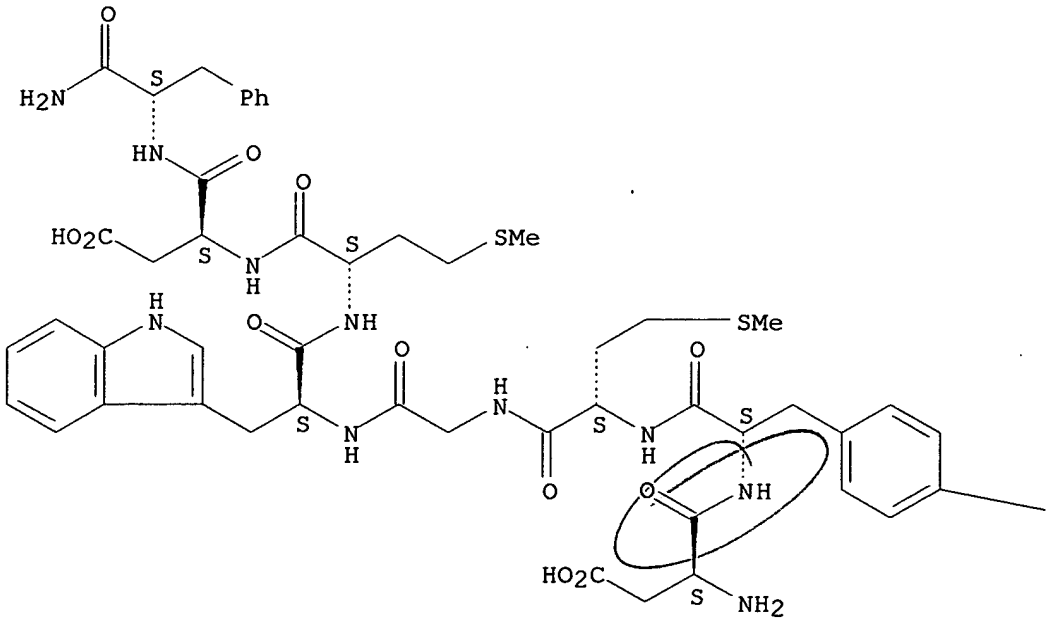




L27 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1986:435752 CAPLUS
DN 105:35752
TI Cholecystokinin analogs containing non-coded amino acids
AU Kovacs, Kalman; Toth, Gabor K.; Zarandi, Marta; Penke, Botond; Kadar, Tibor; Telegdy, Gyula; Hajnal, Ferenc; Lonovics, Janos
CS Dep. Med. Chem., Szeged Univ., Szeged, Hung.
SO Pept.: Struct. Funct., Proc. Am. Pept. Symp., 9th (1985), 583-6
CODEN: 54ZNAJ
DT Conference
LA English
AB Tetragastrin [1947-37-1] and analogs substituted at position 1 with iminodiacetic acid (IDA) and cholecystokinin octapeptide (CCK-8) [**25126-32-3**] and analogs substituted in positions 2 or 7 with p-sulophenylalanine were prepd. and tested for their effects on acid secretion by the rat stomach (gastrin-like effect), on rabbit gallbladder strips (CCK-like effect), and on convulsions [central nervous system (CNS) effects]. Substitution of CCK-8 at position 2 with p-sulfophenylalanine had no effect on biol. activity, but this substitution at position 7 decreased the CCK-like effect with no change in CNS activity. Substitution of IDA at position 1 in tetragastrin eliminated gastrin-like activity but increased CNS activity. The results are interpreted to indicate differences in central and peripheral gastrin and CCK receptors.
IT **25126-32-3 25126-32-3D**, sulfophenylalanine analogs
102986-05-0
RL: BIOL (Biological study)
(**anticonvulsive** and cholecystokinin-like and gastrin-like activities of, structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



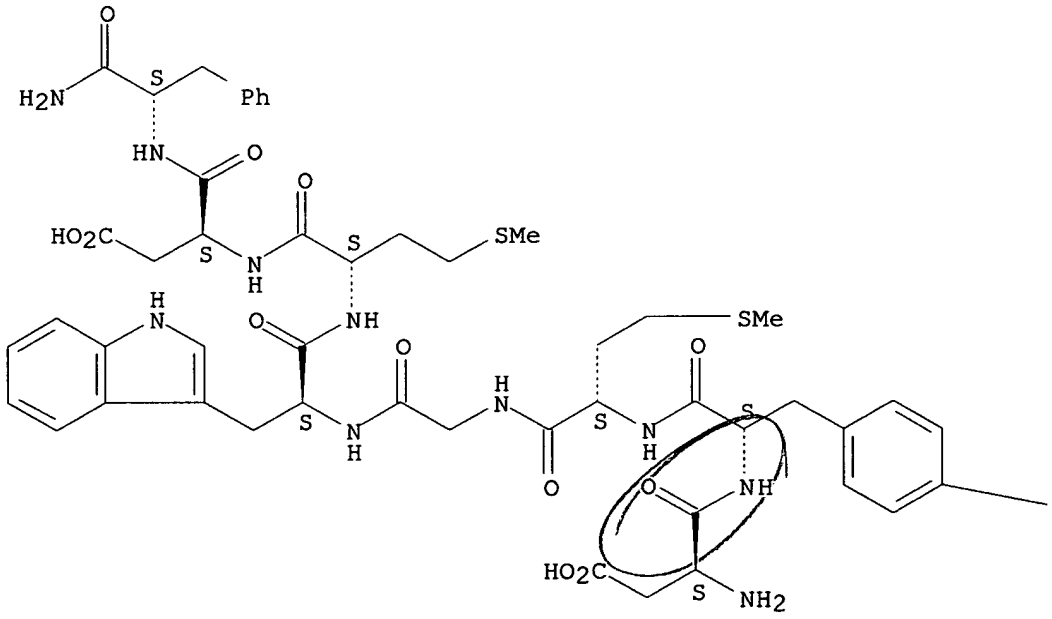
PAGE 1-B

—OSO_3H

RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



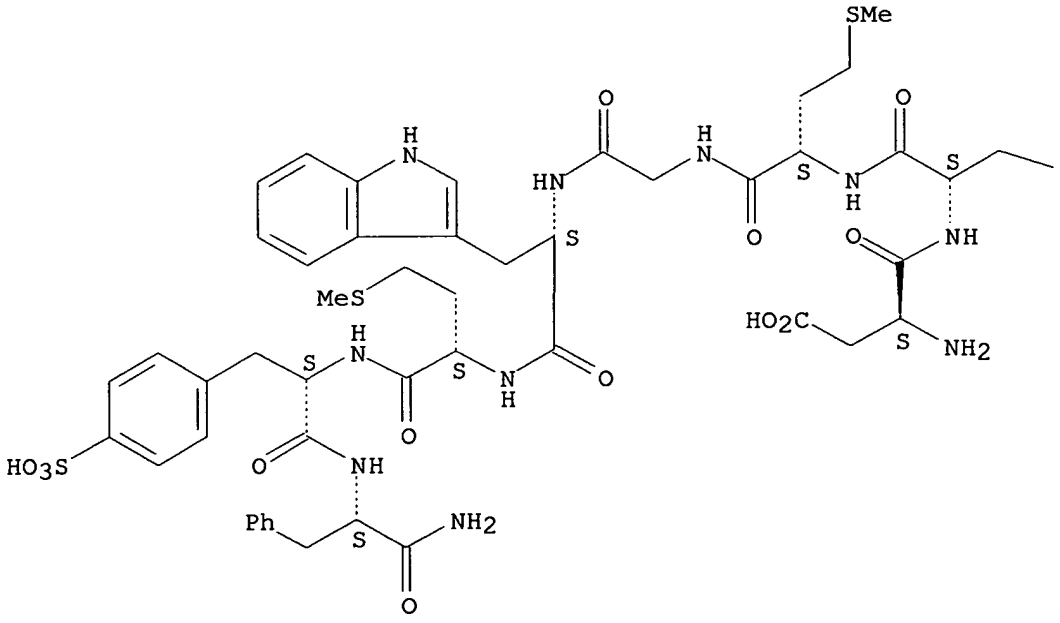
PAGE 1-B

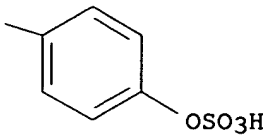
—OSO_3H

RN 102986-05-0 CAPLUS
CN Caerulein, 1-de(5-oxo-L-proline)-2-de-L-glutamine-5-L-methionine-9-(4-sulfo-L-phenylalanine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

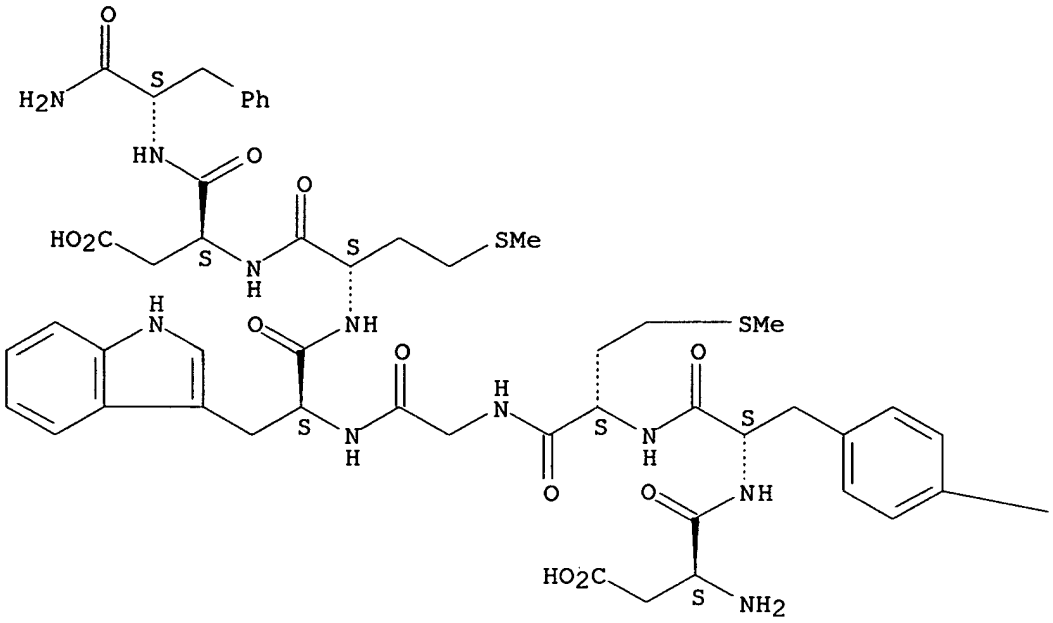



OSO3H

L27 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1986:142735 CAPLUS
DN 104:142735
TI Multiple treatment potentiates the **anticonvulsive** activity of cholecystokinin octapeptides
AU Kadar, Tibor; Penke, Botond; Pesti, Anna; Telegdy, Gyula
CS Dep. Pathophysiol., Univ. Med. Sch., Szeged, H-6701, Hung.
SO Peptides (New York, NY, United States) (1985), 6(6), 1009-14
CODEN: PPTDD5; ISSN: 0196-9781
DT Journal
LA English
AB The dose-response curves for the **anticonvulsive** activity of cholecystokinin octapeptide (CCK-8) [**25126-32-3**] and nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**] against picrotoxin-induced (6 mg/kg s.c.) seizures were assessed either following or without pretreatment with a single high dose of CCK-8 or CCK-8-NS, to examine acute tolerance to the effect after i.p. injections in mice. As CCK-8 or CCK-8-NS pretreatment, a 1.6 .mu.mol/kg dose was injected 2 h prior to 2nd injection. No acute tolerance to the **anticonvulsive** activity was demonstrated, and CCK-8-NS pretreatment potentiated its own **anticonvulsive** activity. Chronic (8-day) daily treatment with a 0.16 .mu.mol/kg dose of CCK-8 or CCK-8-NS antagonized seizures by picrotoxin, presumably in a cumulative manner. To investigate the interactions of CCK octapeptides with other **anticonvulsive** agents, picrotoxin-induced seizures were antagonized with several doses of diazepam [439-14-5] following or without acute, high-dose pretreatment with CCK-8 or CCK-8-NS. The 2 octapeptides only slightly modified the action of diazepam: CCK-8 pretreatment displayed a tendency to antagonize it, whereas CCK-8-NS pretreatment to potentiate it. Apparently, multiple treatment with CCK-8 induces sensitization of CCK receptors mediating **anticonvulsive** activity.
IT **25126-32-3 25679-24-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, sensitization of)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

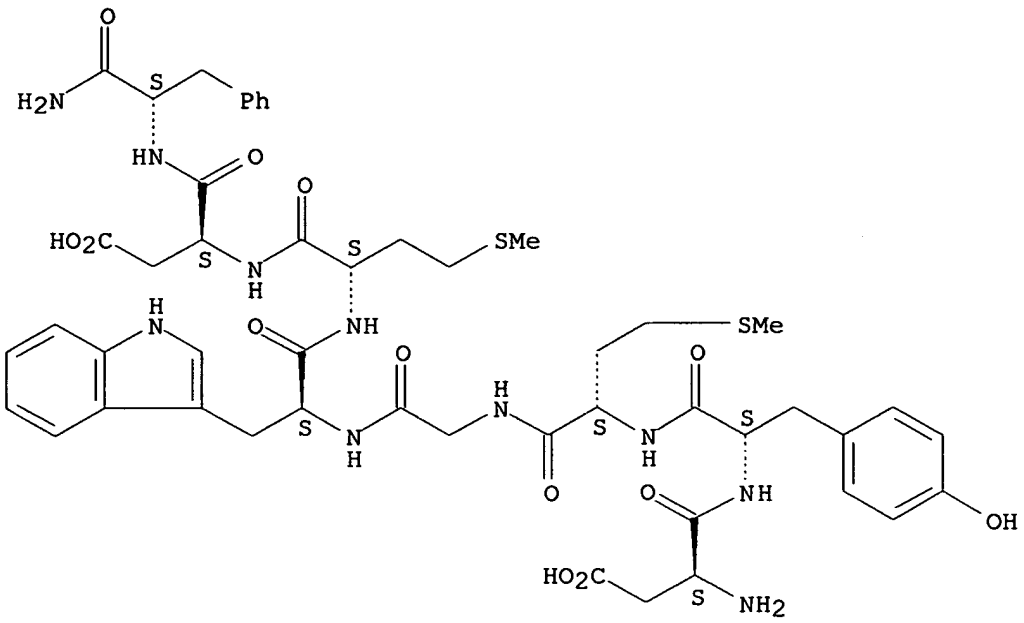


PAGE 1-B

—OSO3H

RN 25679-24-7 CAPLUS
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

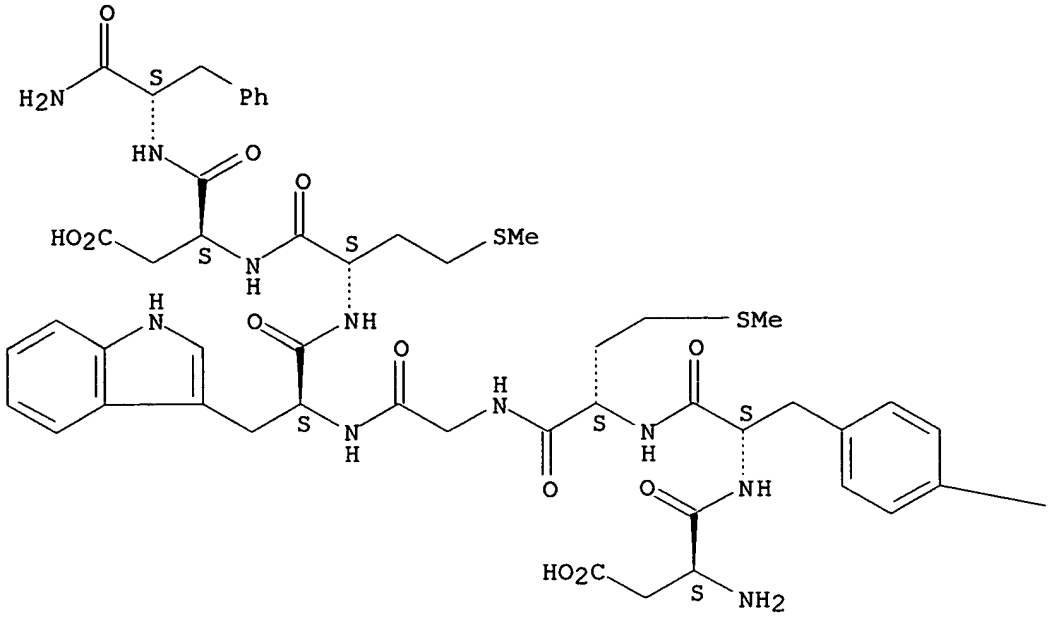
Absolute stereochemistry.



L27 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1985:179251 CAPLUS
DN 102:179251
TI Effects of cholecystokinin octapeptides and their fragments on seizures induced by different **convulsive** drugs
AU Kadar, T.; Pesti, A.; Toth, G.; Penke, B.; Telegdy, G.
CS Dep. Pathophysiol., Univ. Med. Sch., Szeged, Hung.
SO Neuropept. Psychosom. Processes, Int. Conf. Integr. Neurohumoral Mech. (1983), Meeting Date 1982, 231-8. Editor(s): Endroczi, Elember. Publisher: Akad. Kiado, Budapest, Hung.
CODEN: 53HNAO
DT Conference
LA English
AB The antagonist activities of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [**25126-32-3**], nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**] and fragments of these mols. on **convulsive** seizures induced by pentetrazole [54-95-5], strychnine [57-24-9], and picrotoxin [124-87-8] were examd. in mice and rats. Peptides were administered i.p. to mice and intracerebroventricularly to rats, 10 min before administration of the convulsant drug. CCK-8-SE and CCK-8-NS antagonized picrotoxin-induced seizures in both mice and rats, but had no effect on strychnine and pentetrazole-induced convulsions. In both species the octapeptide fragments which attenuated picrotoxin-induced seizures or prolonged the time until death contained the C-terminal tetrapeptide amide (CCK-5-8 [1947-37-1]) sequence of the mol. The C-terminal tripeptide (CCK-6-8 [5934-92-9]) and dipeptide (CCK-7-8 [5241-71-4]) had no **anticonvulsive** activity. The N-terminal nonsulfated tetrapeptide (CCK-1-4-NS [**80790-40-5**]) also slightly antagonized the effect of picrotoxin, but only in rats.
IT **25126-32-3 25679-24-7 80790-40-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, structure in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

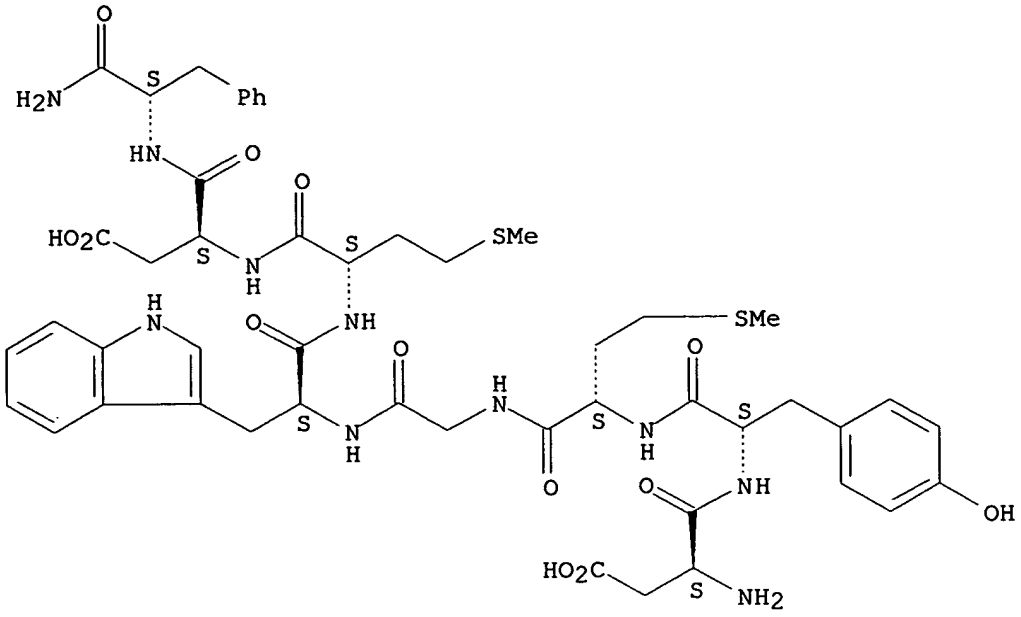


PAGE 1-B

—OSO3H

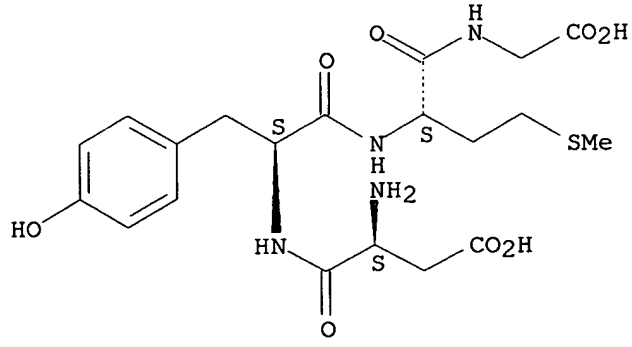
RN 25679-24-7 CAPLUS
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 80790-40-5 CAPLUS
CN Glycine, L-.alpha.-aspartyl-L-tyrosyl-L-methionyl- (9CI) (CA INDEX NAME)

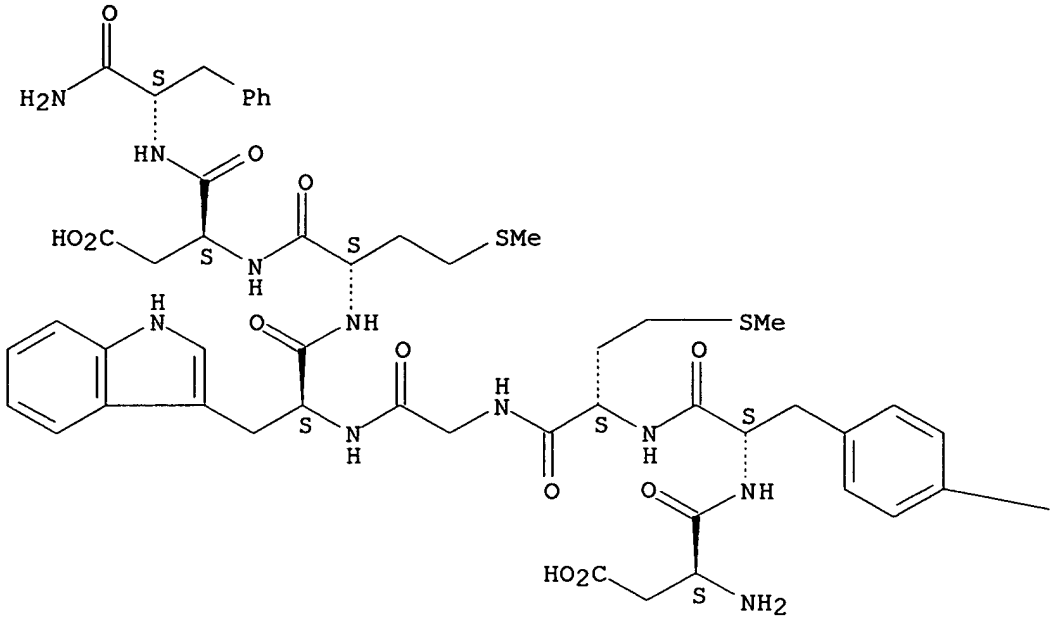
Absolute stereochemistry.



L27 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1984:564133 CAPLUS
DN 101:164133
TI Inhibition of seizures induced by picrotoxin and electroshock by cholecystokinin octapeptides and their fragments in rats after intracerebroventricular administration
AU Kadar, T.; Pesti, A.; Penke, B.; Telegdy, G.
CS Univ. Med. Sch., Inst. Pathophysiol., Szeged, H-6701, Hung.
SO Neuropharmacology (1984), 23(8), 955-61
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB The **anticonvulsive** activity of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [**25126-32-3**], nonsulfated cholecystokinin octapeptide (CCK-8-NS) [**25679-24-7**], and 3 different N- and C-terminal fragments were investigated against seizures induced by picrotoxin [124-87-8] and electroshock in rats after intracerebroventricular administration. Doses of 0.8 and 80 pmol of CCK-8-SE and CCK-8-NS enhanced the latency of seizures induced by picrotoxin and shortened the duration of the clonic phase of the seizures induced by electroshock. Only CCK-8-SE shortened the recovery time and only 0.8 pmol of CCK-8-SE shortened the duration of the tonic phase of convulsions induced by electroshock. Doses of the octapeptides of 8000 pmol were ineffective, with the exception of CCK-8-NS in the picrotoxin test. Of the fragments tested, the C-terminal tetrapeptide (CCK-5-8) [1947-37-1] enhanced the latency of seizures induced by picrotoxin in a dose of 0.8 pmol, and had a dose-dependent biphasic effect on the duration of the clonic phase of seizures induced by electroshock. Intracerebroventricular administration of diazepam [439-14-5] enhanced only the latency of tremor and clonic seizures induced with picrotoxin in a dose of 40 nmol. Twelve nmole of diazepam shortened the clonic phase of convulsions induced by electroshock. The peptides tested were much more active than diazepam, and their EDs were comparable to the amts. of cholecystokinin octapeptide found in brain structures.
IT **25126-32-3 25126-32-3D**, fragments **92510-63-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, after brain administration)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



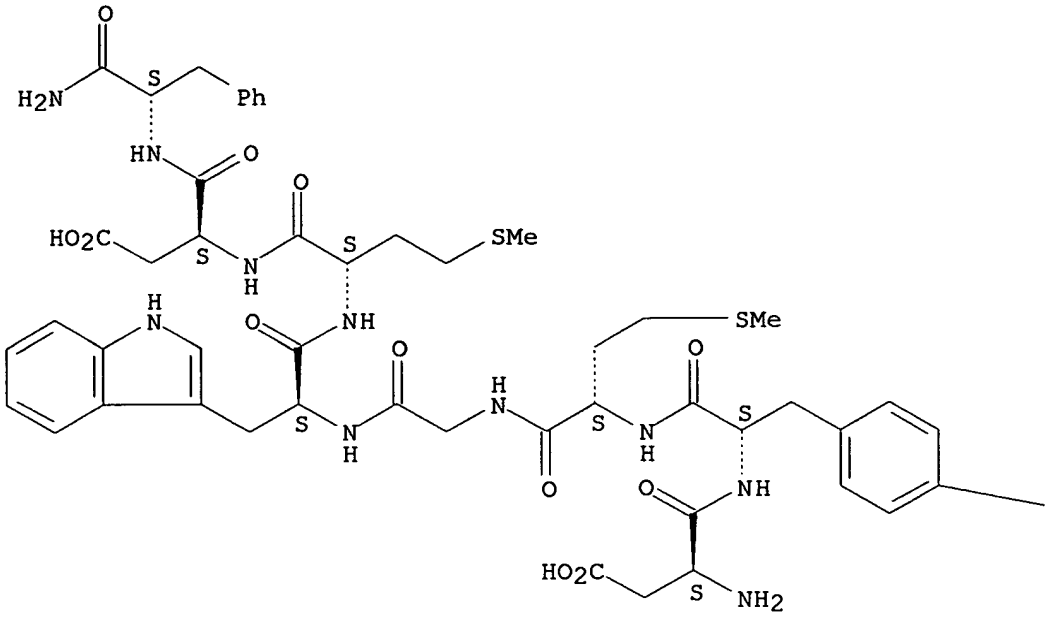
PAGE 1-B

—OSO3H

RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

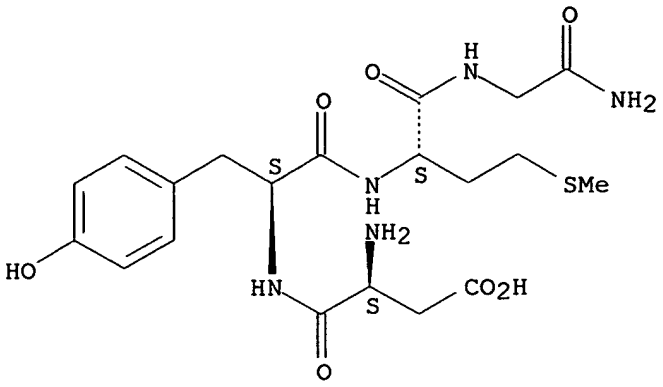


PAGE 1-B

—OSO3H

RN 92510-63-9 CAPLUS
CN Glycinamide, L-.alpha.-aspartyl-L-tyrosyl-L-methionyl- (9CI) (CA INDEX NAME)

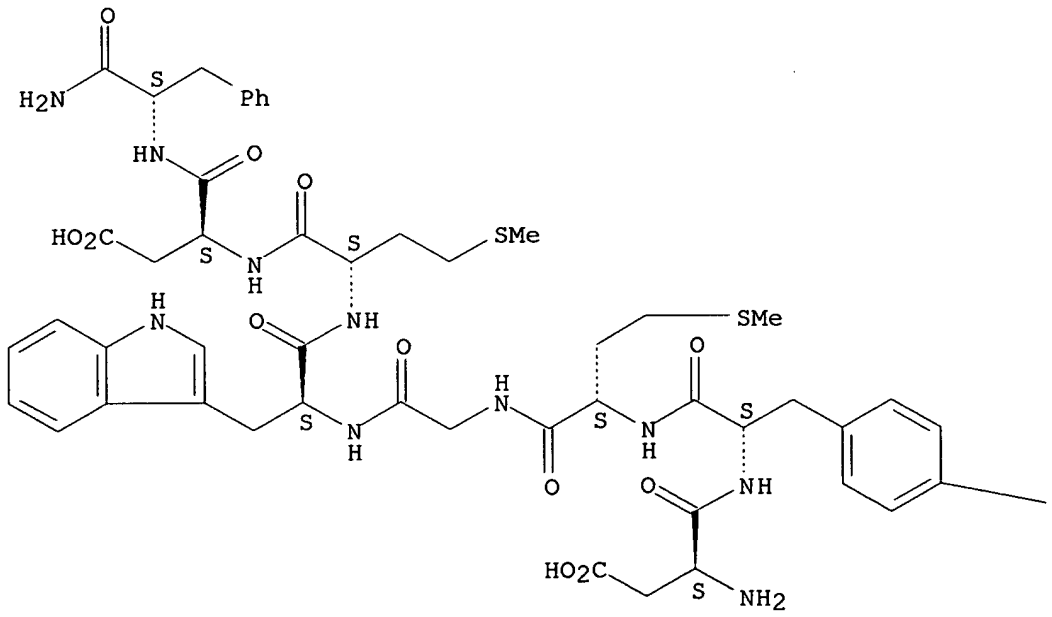
Absolute stereochemistry.



L27 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1982:156064 CAPLUS
DN 96:156064
TI Cerulein and cholecystokinin octapeptide (CCK-8): sedative and **anticonvulsive** effects in mice unaffected by the benzodiazepine antagonist Ro 15-1788
AU Zetler, G.
CS Inst. Pharmakol., Med. Hochsch. Luebeck, Luebeck, D-2400, Fed. Rep. Ger.
SO Neuroscience Letters (1982), 28(3), 287-90
CODEN: NELED5; ISSN: 0304-3940
DT Journal
LA English
AB cholecystokinin octapeptide (CCK-8) [**25126-32-3**], caerulein [17650-98-5], and diazepam [439-14-5] inhibited exploratory rearing activity and harman-induced convulsions in mice. Pretreatment with the selective benzodiazepine receptor antagonist Ro 15-1788 [78755-81-4] reduced or abolished the sedative and **anticonvulsive** effects of diazepam, but left the same effects of both peptides unaffected. The peptide-induced ptosis was even increased by Ro 15-1788. Evidently, the CCK-like peptides do not directly interact with the benzodiazepine receptor.
IT **25126-32-3**
RL: BIOL (Biological study)
(anticonvulsant and sedative action of, benzodiazepine receptor in relation to)
RN 25126-32-3 CAPLUS
CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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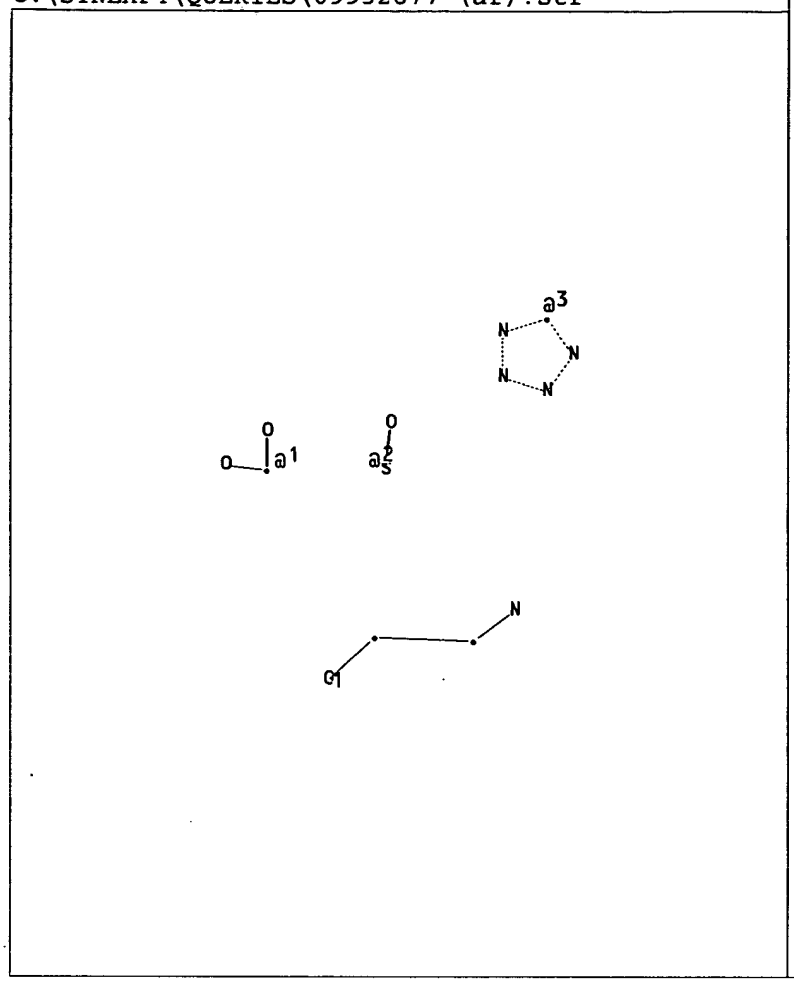

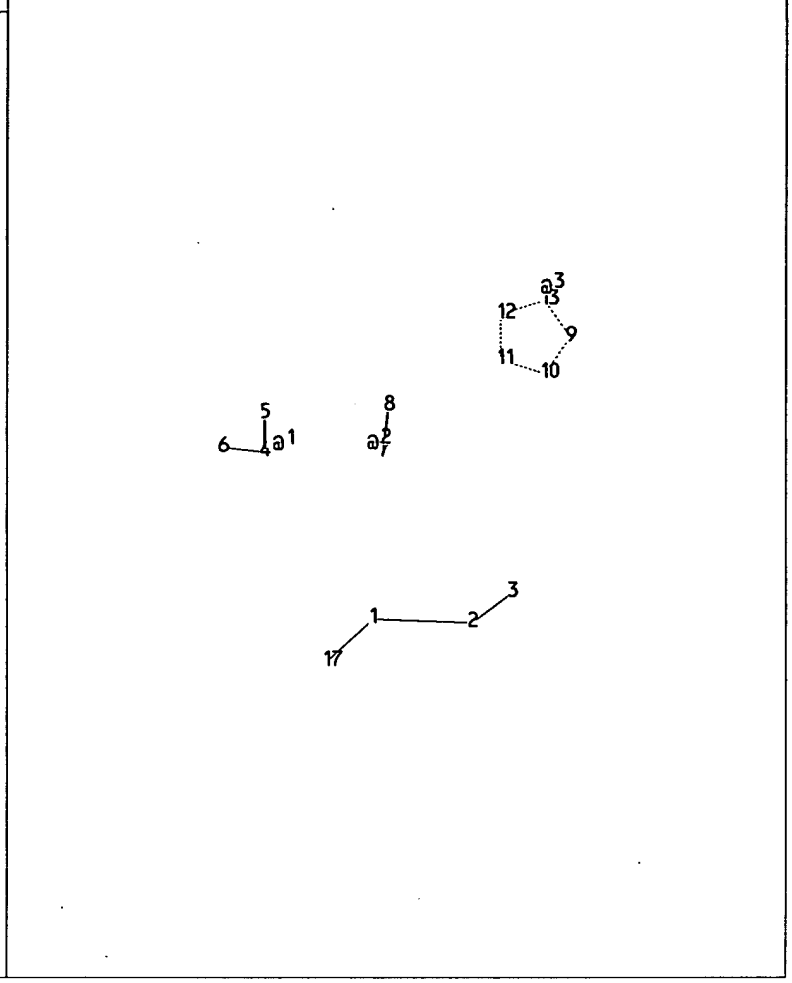

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ring nodes :
9 10 11 12 13
ring/chain nodes :
3
chain bonds :
1-2 1-17 2-3 4-5 4-6 7-8
ring bonds :
9-10 9-13 10-11 11-12 12-13
exact/norm bonds :
1-17 2-3 4-5 4-6 7-8 9-10 9-13 10-11 11-12 12-13
exact bonds :
1-2
isolated ring systems :
containing 9 :

G1:P,COOH,CSSH,PO3H2,OPO3H2,SO2,OSO3H,SO3H,[*1],[*2],[*3]

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 17:CLASS

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L1      STRUCTURE UPLOADED

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L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
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                        BATCH   **INCOMPLETE**
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PROJECTED ANSWERS:          412525 TO   429861

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L3         8310 EPILEPT?

=> s amin? (p) anion?
        1535398 AMIN?
         331349 ANION?
L4        27044 AMIN? (P) ANION?

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L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2001:581740 CAPLUS
DN 135:157692
TI Pharmaceutical compositions for treating hyperhomocysteinaemia caused by drugs
IN Westphal, Sabine; Dierkes, Jutta; Luley, Klaus
PA Germany
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001056609	A1	20010809	WO 2000-EP8801	20000908
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 10004651	A1	20010816	DE 2000-10004651	20000203
PRAI	DE 2000-10004651	A	20000203		

AB The invention relates to a pharmaceutical compn. for producing H2-receptor blockers (cimetidine), non-steroidal analgesics (ibuprofen, indometacin), antidepressants (lithium), anti-**epileptic** agents (phenytoin, carbamazepin), immunosuppressants (cyclosporin, methotrexate), methylxanthine (theophyllin), biguanides (metformin) and lipid reducers (fibrates, **anion** exchangers, nicotinic acid and nicotinic acid analogs) or drugs for treating hypertension, contg. a combination of a pharmaceutical active agent which causes hyperhomocysteinemia and at least one of the following active agents: cobalamine (cyano-, hydroxo-, methyl-), folic acid (pteroylglutamic acid, methyltetrahydrofolate, folinic acid), vitamin B6 (pyridoxine chloride), betaine or N-acetylcysteine. According to a novel observation, hyperhomocysteinemia (a high level of the **amino** acid homocysteine in the blood plasma) is caused by the intake of drugs for lowering blood pressure (diuretics, calcium antagonists, ACE inhibitors or angiotensin-II receptor antagonists), non-steroidal analgesics, antidepressants (lithium), immunosuppressants, methylxanthine (theophyllin), biguanides (metformin) or lipid reducers (fibrates, **anion** exchangers, nicotinic acid and nicotinic acid analogs). Thus a dragee contained: hydrochlorothiazide 25 mg; cyanocobalamine 1000 .mu.g; pteroylglutamic acid 100 .mu.g; pyridoxine chloride 2 mg; and excipients.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1998:621100 CAPLUS
DN 129:239901
TI Anti-epileptogenic agents, and preparation thereof
IN Weaver, Donald F.; Milne, Paul H.; Tan, Christopher Y. K.; Carran, John R.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English

Applicant's

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840055	A2	19980917	WO 1998-CA244	19980312
	WO 9840055	A3	19990218		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6306909	B1	20011023	US 1998-41371	19980311
	AU 9864923	A1	19980929	AU 1998-64923	19980312
	EP 969823	A2	20000112	EP 1998-910555	19980312
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 337849	A	20000128	NZ 1998-337849	19980312
	JP 2001515483	T2	20010918	JP 1998-539010	19980312
	US 2002025949	A1	20020228	US 2001-932676	20010816
PRAI	US 1997-41140P	P	19970312		
	US 1998-73536P	P	19980203		
	US 1998-41371	A3	19980311		
	WO 1998-CA244	W	19980312		

OS MARPAT 129:239901
AB Methods and compds. useful for the inhibition of convulsive disorders, including epilepsy, are disclosed. The methods and compds. of the invention inhibit or prevent ictogenesis and epileptogenesis. Methods for prepg. the compds. of the invention are also described.

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1995:714561 CAPLUS
DN 123:159959
TI New immunoassay techniques using Nafion-modified electrodes and cationic redox labels or enzyme labels
AU Le Gal La Salle, A.; Limoges, B.; Rapicault, S.; Degrand, C.; Brossier, P.
CS Universite Blaise Pascal, Thermodynamique et Electrochimie en Solution (U.R.A. 434), Laboratoire d'Electrochimie Organique, 24 Avenue des Landais, Aubiere, 63 177, Fr.
SO Analytica Chimica Acta (1995), 311(3), 301-8
CODEN: ACACAM; ISSN: 0003-2670
PB Elsevier
DT Journal
LA English
AB Two new competitive immunoassay techniques with sensitive electrochem. detection at Nafion film modified electrodes are described and compared. Method A implies the use of an antigen labeled with a cationic redox group in homogeneous immunoassay. Method B involves an enzyme-labeled antigen, in connection with an **anionic** substrate+cationic electroactive product of the enzymic reaction in heterogeneous assay. A 5 min accumulation step precedes the electrochem. detection in both methods. Method B can be applied to the detn. of any kind of antigen, whereas method A is restricted to haptens. Phenytoin, an anti-**epileptic** drug, was chosen as a model antigen and labeled by cobaltocenium and alk. phosphatase to illustrate methods A and B, resp. The enzymic reaction was performed with (N-ferrocenoyl)-6-**amino**-2,4-dimethylphosphate as substrate in method B. The dianionic substrate was repulsed from the Nafion film, whereas the corresponding enzymically generated alc. was selectively entrapped within the film as a ferricinium salt by applying a potential of 0.6 V vs. Ag/AgCl during the accumulation step performed at pH 7.4. Both methods were tested for the detn. of phenytoin in clin. serum samples.

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=> s convuls?
L6       21555 CONVULS?

=> d his

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L2            50 S L1 SSS SAM

     FILE 'CAPLUS' ENTERED AT 16:06:26 ON 10 APR 2003
L3          8310 S EPILEPT?
L4         27044 S AMIN? (P) ANION?
L5             3 S L3(P)L4
L6         21555 S CONVULS?

=> s l4(p)l6
L7           20 L4(P)L6

=> d l7 1-20 bib,ab
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L7 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 2002:239707 CAPLUS
DN 136:380282
TI Identification of a novel residue within the second transmembrane domain that confers use-facilitated block by picrotoxin in glycine .alpha.1 receptors
AU Dibas, Mohammed I.; Gonzales, Eric B.; Das, Paromita; Bell-Horner, Cathy L.; Dillon, Glenn H.
CS Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, 76107, USA
SO Journal of Biological Chemistry (2002), 277(11), 9112-9117
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The central nervous system **convulsant** picrotoxin (PTX) inhibits GABAA and glutamate-gated Cl- channels in a use-facilitated fashion, whereas PTX inhibition of glycine and GABAC receptors displays little or no use-facilitated block. We have identified a residue in the extracellular aspect of the second transmembrane domain that converted picrotoxin inhibition of glycine .alpha.1 receptors from non-use-facilitated to use-facilitated. In wild type .alpha.1 receptors, PTX inhibited glycine-gated Cl- current in a competitive manner and had equiv. effects on peak and steady-state currents, confirming a lack of use-facilitated block. Mutation of the second transmembrane domain 15'-serine to glutamine (.alpha.1(S15'Q) receptors) converted the mechanism of PTX blockade from competitive to non-competitive. However, more notable was the fact that in .alpha.1(S15'Q) receptors, PTX had insignificant effects on peak current amplitude and dramatically enhanced current decay kinetics. Similar results were found in .alpha.1(S15'N) receptors. The reciprocal mutation in the .beta.2 subunit of .alpha.1.beta.2 GABAA receptors (.alpha.1.beta.2(N15'S) receptors) decreased the magnitude of use-facilitated PTX inhibition. Our results implicate a specific **amino** acid at the extracellular aspect of the ion channel in detg. use-facilitated characteristics of picrotoxin blockade. Moreover, the data are consistent with the suggestion that picrotoxin may interact with two domains in ligand-gated **anion** channels.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 2001:300390 CAPLUS
DN 135:239880
TI Significance of reactive oxygen in kidney disease elucidated by [measuring changes in] uremic toxins
AU Aoyagi, Kazumasa
CS Department of Internal Medicine, University of Tsukuba, Tsukuba, 305-8575, Japan
SO Journal of Artificial Organs (2001), 4(1), 3-7
CODEN: JAORFN; ISSN: 1434-7229
PB Springer-Verlag Tokyo
DT Journal; General Review
LA English
AB A review with 24 refs. Synthesis of guanidinosuccinic acid (GSA) and methylguanidine (MG) is markedly increased in end-stage renal disease, and these substances are known as uremic toxins. GSA has been identified as one of the major causes of bleeding tendency; it is a Na-K ATPase inhibitor and the cause of **convulsions** in end-stage kidney failure. Recently, GSA has been found to be an activator of the N-methyl-D-aspartate (NMDA) receptor that generates NO and plays an important role in nerve development and the death of neurons. In peripheral nerves, it functions in pain and itching sensations. GSA is formed from argininosuccinate and the hydroxyl radical. The combination of NO and superoxide **anion** also generates GSA. Thus, in the system involving the GSA-NMDA receptor-NO + O2-, GSA may act as an amplifier of reactive O generation. MG, another major uremic toxin, causes hypertension and shortening of the lifespan. MG is formed through the hydroxyl adduct of creatinine (creatol). Therefore, MG and/or creatol can be used to est. hydroxyl radical generation. A marked increase of creatol synthesis has been reported in severely hyperparathyroid patients. Addnl., this method has been used to demonstrate an increase in hydroxyl radical generation by puromycin **aminonucleoside** (PAN), which induces severe proteinuria. Further, the increased hydroxyl radical generation induced by PAN is caused by the activation of calcium-dependent protein kinase C and is prevented by inhibitors of this enzyme. Increased hydroperoxides in PAN-treated glomeruli have also been shown. Thus, increases in MG and GSA may indicate hydroxyl radical generation in renal failure.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 2001:34967 CAPLUS
DN 134:189215
TI Significance of reactive oxygen in kidney disease elucidated by uremic toxins: from uremia to nephrosis
AU Aoyagi, Kazumasa
CS Department of internal medicine, University of Tsukuba, Ibaraki, 305-8575, Japan
SO Free Radicals in Chemistry, Biology and Medicine (2000), 396-402.
Editor(s): Yoshikawa, Toshikazu. Publisher: OICA International (UK) Ltd., London, UK.
CODEN: 69AUUF
DT Conference
LA English
AB The major pathway to form guanidino compds. is via the urea cycle. About 0.5 mol/day of argininosuccinic acid (ASA) and arginine are formed in man and converted to urea. Many guanidino compds. those syntheses increased in end stage renal disease (ESRD) are toxic. Guanidinosuccinic acid (GSA, N-amidino-L-aspartate) has been identified as the major cause of bleeding tendency, a Na-K ATPase inhibitor and cause of **convulsions** in ESRD. GSA activates N-methyl-D-aspartate (NMDA) receptor that generates NO and plays an important role in nerve development and the death of neurons. In peripheral nerves, it functios in pain sensation and itching. GSA is formed from ASA and the hydroxyl radical. Conbination of NO and superoxide **anion** (O2) also generates GSA. Thus, in the system involving the GSA-NMDA receptor-NO+O2, GSA may act as an amplifier of reactive oxygen generation. Methylguanidine(MG), another major uremic toxin, causes hypertension and a shortening of the life span. MG is formed through the hydroxyl adduct of creatinine (creatol). Therefore, MG and/or creatol can be used to est. hydroxyl radical generation. This method demonstrated an increase in hydroxyl radical generation by puromycin **aminonucleoside** (PAN) which induces heavy proteinuria. Increased hydroxyl radical generation induced by PAN is caused by the activation of calcium-dependent protein kinase C (PKC) and is prevented by the inhibitors of PKC. Increased hydroperoxides in PAN treated glomeruli was shown. Thus, guanidino compds. act as the toxic substance as well as the indicator of hydroxyl radical generation caused by protein kinase C activation.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 2000:545423 CAPLUS
DN 133:358747
TI The influence of transmembrane **amino** acid residues on allosteric modulation of transmitter-gated **anion** channels by **convulsants** and general anesthetics
AU Belelli, D.; Peters, J. A.; Lambert, J. J.
CS Department of Pharmacology and NeuroScience, NeuroScience Institute, Ninewells Hospital and Medical School, University of Dundee, Dundee, DD1 9SY, UK
SO Chloride Channels (1999), 161-175. Editor(s): Kozlowski, Roland Z. Publisher: Isis Medical Media Ltd., Oxford, UK.
CODEN: 69AGBM
DT Conference; General Review
LA English
AB A review with 65 refs. The family of inhibitory transmitter-gated channels includes the vertebrate GABAA and glycine receptors, and the invertebrate GABA- and glutamate-gated **anion** channels [1]. Although they exhibit limited overall identity in primary **amino** acid sequence, a degree of conservation is apparent for the regions of the polypeptides that comprise the four transmembrane (TM) domains and the channel lining TM2 segment in particular [1]. Recent mutagenesis expts. have emphasized the role of structurally homologous **amino** acids located within the TM2 domain as determinants of the actions of a structurally diverse group of agents that act either to inhibit or enhance receptor function. In this chapter, we describe how specific **amino** acid residues influence the effects of chem. **convulsants** and general anesthetics at transmitter-gated **anion** channels and consider whether changes in function reflect binding or transductional phenomena.
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1998:753650 CAPLUS
DN 130:119507
TI Bimodal action of furosemide on convulsant [3H]EBOB binding to cerebellar and cortical GABAA receptors
AU Maksay, Gabor; Korpi, Esa R.; Uusi-Oukari, Mikko
CS Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, 1525, Hung.
SO Neurochemistry International (1998), 33(4), 353-358
CODEN: NEUIDS; ISSN: 0197-0186
PB Elsevier Science Ltd.
DT Journal
LA English
AB Picrotoxinin-sensitive binding of a **convulsant** 4'-ethynyl-4-n-[2,3-3H2]propyl-bicycloorthobenzoate ([3H]EBOB) to .gamma.-**aminobutyric** acid type A (GABAA) receptors was characterized in rat cerebrocortical and cerebellar membranes. The non-penetrating org. **anions**, furosemide and niflumate, in spite of their structural similarities, exerted differential effects on [3H]EBOB binding. Furosemide, a loop diuretic and a specific antagonist of a cerebellar GABAA receptor population, and GABA decreased the inhibitory potencies of each other in the cerebellum, while enhanced them in the cortex. The inhibitory potencies of niflumate, an anti-inflammatory and a chloride channel blocker, and GABA were enhanced by each other both in the cerebellum and cortex. Removal of chloride ions did not modify the effects of furosemide on [3H]EBOB binding. Furosemide antagonized the inhibition of cerebellar [3H]EBOB binding by a low pentobarbital concn. (0.1 mM), but enhanced the inhibition by a high concn. (0.5 mM). The results indicate that [3H]EBOB binding can be used to detect the known pharmacol. features of the cerebellar granule cell-specific .alpha.6 subunit-contg. GABAA receptors. The data extends the properties of furosemide antagonism of this receptor subtype of chloride insensitivity and interactions with barbiturate sites.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1998:621100 CAPLUS
DN 129:239901
TI Anti-epileptogenic agents, and preparation thereof
IN Weaver, Donald F.; Milne, Paul H.; Tan, Christopher Y. K.; Carran, John R.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840055	A2	19980917	WO 1998-CA244	19980312
	WO 9840055	A3	19990218		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6306909	B1	20011023	US 1998-41371	19980311
	AU 9864923	A1	19980929	AU 1998-64923	19980312
	EP 969823	A2	20000112	EP 1998-910555	19980312
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 337849	A	20000128	NZ 1998-337849	19980312
	JP 2001515483	T2	20010918	JP 1998-539010	19980312
	US 2002025949	A1	20020228	US 2001-932676	20010816
PRAI	US 1997-41140P	P	19970312		
	US 1998-73536P	P	19980203		
	US 1998-41371	A3	19980311		
	WO 1998-CA244	W	19980312		

OS MARPAT 129:239901
AB Methods and compds. useful for the inhibition of convulsive disorders, including epilepsy, are disclosed. The methods and compds. of the invention inhibit or prevent ictogenesis and epileptogenesis. Methods for prepg. the compds. of the invention are also described.

L7 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1994:244661 CAPLUS
DN 120:244661
TI Process for the preparation of 1-unsubstituted 3-aminopyrroles with CNS activity
IN Rolfs, Andreas; Liebscher, Jeurgen; Unverferth, Klaus; Faust, Gottfried
PA Arzneimittelwerk Dresden G.m.b.H., Germany
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 583561	A2	19940223	EP 1993-108826	19930602
	EP 583561	A3	19940706		
	EP 583561	B1	19980401		
	R: AT, BE, CH, DE, ES, FR, GB, IE, IT, LI, NL, PT, SE				
	DE 4227479	A1	19940224	DE 1992-4227479	19920820
	AT 164573	E	19980415	AT 1993-108826	19930602
	JP 06211784	A2	19940802	JP 1993-185132	19930727
	US 5414082	A	19950509	US 1993-104795	19930811
	CA 2104085	AA	19940221	CA 1993-2104085	19930813
	CN 1087628	A	19940608	CN 1993-116710	19930820
PRAI	DE 1992-4227479		19920820		

OS CASREACT 120:244661; MARPAT 120:244661
AB Title pyrroles I [R1 = H, alk(en)yl, (hetero)aryl, NO2, cyano, acyl, alkoxycarbonyl, **aminocarbonyl**, aryloxycarbonyl, sulfonyl group; R2, R3 = H, optionally heteroatom-substituted aryl or alkyl; or R2R3 = alkylene optionally contg. heteroatoms or substituted; R4, R5 = H, alkoxycarbonyl, **amino**(thio)carbonyl, (un)substituted alkyl or (hetero)aryl] are prepd. by ring transformation of isothiazolium salts II [X- = acid **anion**, e.g., halide, ClO4-, BF4-, HSO4-, SO42-, OH-, or CF3SO3-], preferably in the presence of a base. For example, isothiazolium bromide II [R1 = CO2Bu, NR2R3 = morpholino, R4 = C6H4Cl-4, R5 = H, X = Br] was treated with Et3N in boiling EtOH, with pptn. and removal of extruded S, to give title compd. III in 63% yield. A total of 18 I were prepd., with typical yields of 70-90%. Two I at 0.5-1.0 .times. 10-3 mol/kg in the maximal electroconvulsion test in mice gave 80-100% inhibition of **convulsions**.

L7 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1994:125710 CAPLUS
DN 120:125710
TI Inactivation of the convulsant site of the GABAA receptor complex by arginine-specific reagents and its protection by the anion binding sites
AU Maksay, Gabor
CS Cent. Res. Inst. Chem., Hung. Acad. Sci., Budapest, 1525, Hung.
SO Molecular Neuropharmacology (1993), 3(3), 161-5
CODEN: MOLNEO; ISSN: 0959-5244
DT Journal
LA English
AB [35S]t-Butylbicyclophosphorothionate (TBPS) binding to the **convulsant** sites of the .gamma.-**aminobutyric** acid (GABAA) receptor complex was measured in washed membranes prepd. from rat forebrain. A concn.-dependent decrease in TBPS binding was obsd. with pretreatment by arginine-selective reagents in the following order of potency: p-chloro-phenylglyoxal > phenylglyoxal > 2,3-butanedione > 1,2-cyclohexanedione > camphorquinone-10-sulfonic acid. Inactivation by butanedione pretreatment was attenuated by sodium salts of the Eccles **anions** chloride and bromide. Tartarate and sulfate salts were ineffective. The decrease in TBPS binding by butanedione pretreatment could not be prevented by GABA or by picrotoxinin, a ligand of the **convulsant** sites. Pretreatment of the membranes at 30.degree. with sodium bromide resulted in a concn.-dependent increase in TBPS binding (EC50 = 63 mM). The submaximally enhancing effect of 250 nM sodium bromide was amplified by GABA and attenuated by the GABAA antagonist SR 95531. It is concluded that arginine residues might participate in the binding of Eccles **anions** at the mouths of the GABAA-chloride ionophores.

L7 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1994:24143 CAPLUS
DN 120:24143
TI Interconvertible kinetic states of t-butylbicycloorthobenzoate binding sites of the .gamma.-aminobutyric acidA ionophores
AU Maksay, Gabor; van Rijn, Clementina M.
CS Central Res. Inst. Chem., Hung. Acad. Sci., Budapest, Hung.
SO Journal of Neurochemistry (1993), 61(6), 2081-8
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
AB The kinetics of t-[3H]butylbicycloorthobenzoate (TBOB) binding to the **convulsant** sites of the .gamma.-**aminobutyric** acidA (GABAA) receptor-ionophore complex were examd. in synaptosomal membrane prepns. of rat brain. On and off rates of TBOB binding were accelerated by 1 .mu.M GABA and decelerated by 1 .mu.M bicuculline methochloride, a GABAA antagonist. The presence of GABA and bicuculline methochloride created rapid and slow phases of dissocn., resp. The three groups of rate consts. distinguished for the dissocn. of 4 nM and 30 nM [3H]TBOB represent multiaffinity states of the **convulsant** sites depending on the presence of GABA or bicuculline methochloride. Apparent assocn. rate consts. do not obey the equation kapp = koff + kon [TBOB] without assuming interconvertibility of the kinetic states during binding. Avermectin B1a (AVM B1a), a chloride channel opening agent, accelerated the assocn. and dissocn. of TBOB and resulted in a biphasic effect on TBOB binding, i.e., enhancement at low concns. (EC50 7.8 nM) followed by displacement at high concns. (IC50 6.3 .mu.M) of AVM B1a. AVM B1a resulted in similar biphasic effects of t-[35S]butylbicyclophosphorothiona te binding. DIDS, an isothiocyanatostilbene deriv. with irreversible **anion** channel blocking effect, selectively inhibited basal [3H]TBOB binding (IC50 125 .mu.M DIDS) leaving the enhancement by AVM B1a unaffected.

L7 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1993:510758 CAPLUS
DN 119:110758
TI Effect of acute pretreatment of lead on picrotoxin-induced convulsions in rats
AU Krishnamoorthy, M. S.; Parthiban, N.; Muthu, P.; Paul, V.; Balagopal, G.; Kumaravel, T. S.
CS Dr. A.L.M. Post Grad. Inst. Basic Med., Univ. Madras, Madras, 600 113, India
SO Journal of Applied Toxicology (1993), 13(3), 155-9
CODEN: JJATDK; ISSN: 0260-437X
DT Journal
LA English
AB The effect of acute exposure to lead acetate (LA)/lead nitrate (LN) on onset and severity of **convulsions** induced by a low dose of picrotoxin was examd. in rats. Both LA and LN reduced the time of onset and exacerbated the severity of **convulsions**, with a resultant high lethality. On comparison, it was noted that in the LA-pretreated group, **convulsion** scores and incidence of tonus and mortality were much higher; the appearance of tonus was more delayed than in the LN-pretreated group. In lead-pretreated animals, the potentiation of picrotoxin-induced **convulsions** was accompanied by higher lead levels in blood. However, the whole-brain lead levels were not significantly different in these animals compared to the controls. The difference in the degree of potentiation by the two forms of lead could possibly be attributed either to the role of a combination of **anions** and cations or to the variable cerebral uptake and regional distribution of lead or due partly to the extent of competitive interaction involving delta-**aminoaevulinic** acid-whose level is known to be elevated consequent to lead-induced disruption of heme biosynthesis-at GABA receptors.

L7 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1987:509924 CAPLUS
DN 107:109924
TI Characterization of GABAA receptor-mediated chlorine-36 ion uptake in rat brain synaptoneurosomes
AU Luu, My Do; Morrow, Leslie; Paul, Steven M.; Schwartz, Rochelle D.
CS Clin. Neurosci. Branch, Natl. Inst. Ment. Health, Bethesda, MD, 20892, USA
SO Life Sciences (1987), 41(10), 1277-87
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB GABA receptor-mediated 36Cl- uptake was measured in synaptoneurosomes from rat brain. GABA and GABA agonists stimulated 36Cl- uptake in a concn.-dependent manner with the following order of potency: muscimol > GABA > piperidine-4-sulfonic acid (P4S) > THIP = 3-**aminopropanesulfonic** acid (3APS) >> taurine. Both P4S and 3APS behaved as partial agonists, whereas the GABAB agonist, baclofen, was ineffective. The response to muscimol was inhibited by bicuculline and picrotoxin in a mixed competitive/non-competitive manner. Other inhibitors of GABA receptor-opened channels or non-neuronal **anion** channels such as penicillin, picrate, furosemide, and disulfonic acid stilbenes also inhibited the response to muscimol. A regional variation in muscimol-stimulated 36Cl- uptake was obsd.; the largest responses were obsd. in the cerebral cortex, cerebellum, and hippocampus, moderate responses were obtained in the striatum and hypothalamus and the smallest response was obsd. in the pons-medulla. GABA receptor-mediated 36Cl- uptake was also dependent on the **anion** present in the media. The muscimol response varied in media contg. the following **anions** : Br- > Cl- .gtoreq. NO3- > I- .gtoreq. SCN- >> C3H5OO- > F-, consistent with the relative **anion** permeability through GABA receptor-gated **anion** channels and the enhancement of **convulsant** binding to the GABA receptor-gated Cl- channel.

L7 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1987:116019 CAPLUS
DN 106:116019
TI The permeability of .gamma.-aminobutyric acid-gated chloride channels is described by the binding of a "cage" convulsant, t-butylbicyclophosphoro[35S]thionate
AU Havoundjian, H.; Paul, S. M.; Skolnick, P.
CS Lab. Bioorg. Chem., Natl. Inst. Arthritis, Diabetes, and Dig. and Kidney Dis., Bethesda, MD, 20892, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1986), 83(23), 9241-4
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The cage **convulsant** t-butylbicyclophosphoro[35S]thionate (I) binds with high affinity to sites at or near a .gamma.-**aminobutyric** acid (GABA)-gated chloride channel according to current hypothesis. The potencies of a series of **anions** in enhancing I binding correlated highly with their relative permeabilities through GABA-gated chloride channels. Furthermore, significant correlations are obtained between the apparent affinity (Kd) of I estd. in the presence of these **anions** and their relative permeabilities through GABA-gated chloride channels. The latter relationships obtained whether the Kd of I as estd. in rat cerebral cortex was correlated with the relative permeabilities of these **anions** in either frog dorsal root ganglion cells or primary cultures of mouse spinal cord neurons. Apparently, I binds to GABA-gated chloride channels and the apparent affinity of this radioligand is directly related to the permeability of these channels. Thus, radioreceptor techniques using I may provide a simple means of describing permeability characteristics of GABA-gated chloride channels.

L7 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1983:401467 CAPLUS
DN 99:1467
TI [35S]t-butylbicyclophosphorothionate binds with high affinity to brain-specific sites coupled to .gamma.-aminobutyric acid-A and ion recognition sites
AU Squires, Richard F.; Casida, John E.; Richardson, Martine; Saederup, Else
CS Rockland Res. Inst., Orangeburg, NY, 10962, USA
SO Molecular Pharmacology (1983), 23(2), 326-36
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
AB 35S-labeled t-butylbicyclophosphorothionate (TBPS)(I) [70636-86-1] binds to specific sites on EDTA/water-dialyzed rat brain P2 membranes, with a dissocn. const. (Kd) near 17 nM, in 200 mM KBr at 25.degree. and pH 7.5. Nonspecific binding is .apprx.33% of total binding using a filtration assay. [35S]TBPS binding is entirely dependent on appropriate salts, with the **anion** playing the predominant role. The optimal temp. for [35S]TBPS specific binding is near 21.degree., with none at 0.degree.. The pH optimum for binding is 7.5-8.5. At 25.degree. in 200 mM KBr, [35S]TBPS (2 nM) assocs. with a major binding site with a half-time near 11 min, and dissocs. in a polyphasic way. The slow component of dissocn. has a half-time near 29 min and constitutes .apprx.70% of the total specific binding. NaCl alone can almost completely protect specific [35S]TBPS binding sites against heat inactivation (30 min, 60.degree.) with 50% of maximal protection near 200 mM and a Hill no. near 1.6. In whole rat forebrain, [35S]TBPS receptor d. is near 50 pmol/g of wet tissue. Receptor d. is higher in cerebral cortex, cerebellum, and hippocampus (50-60 pmol/g) than in hypothalamus, striatum, and pons-medulla (in decreasing order). There is negligible specific binding in the liver, kidney, and lung. The affinities of Eccles **anions** (chloride, bromide, iodide, and thiocyanate) for the binding-enhancement site are selectively reduced by .gamma.-**aminobutyric** acid (GABA) [56-12-2] and all GABA-A receptor agonists tested, but not by baclofen. The affinities of non-Eccles **anions** (fluoride, sulfate, phosphate, and bicarbonate) for the **anion** site are either unaffected or increased by GABA. The inhibitory effects of GABA-A receptor agonists are potently reversed by the bicuculline-like GABA antagonist R 5135. Specifically bound [35S]TBPS is potently displaced (IC50 values <1 .mu.M) by all picrotoxin-like (cage) **convulsants** tested with the exception of p-chlorophenylsilatrane. TBPS, dihydropicrotoxinin, and benzodiazepine binding sites have similar densities and distributions. Specific [35S]TBPS binding is inhibited by several barbiturates with IC50 values in the 30-60 .mu.M range as well as the barbiturate-like substances (+)-etomidate (2.8 .mu.M) and methaqualone (43 .mu.M). The pyrazolopyridines etazolate and cartazolate are highly potent displacers of [35S]TBPS binding (IC50 values <1 .mu.M). The inhibitions of [35S]TBPS binding by barbiturates, etomidate, methaqualone, pyrazolopyridines, EtOH, and meprobamate are all potently, but noncompetitively, reversed by R 5135 (10 nM) whereas the inhibitions by most of the **convulsants** tested are potentiated or unaffected. TBPS probably binds to the same sites as dihydropicrotoxinin but has the advantages of higher affinity and a better signal-to-noise ratio. Many **convulsants**, anticonvulsants, sedatives, hypnotics, and anxiolytics seem to exert their characteristic effects by acting on or near TBPS (picrotoxin) sites, in benzodiazepine/ion/GABA/picrotoxin receptor complexes.

L7 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1983:160585 CAPLUS
DN 98:160585
TI Quaternary derivatives of N-(substituted aminoalkyl)-2-oxo-1-pyrrolidineacetamides as cognition activators
IN L'Italien, Yvon J.
PA Warner-Lambert Co. , USA
SO U.S., 5 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4372960	A	19830208	US 1980-215959	19801212
PRAI	US 1980-215959		19801212		

AB Pyrrolidines I [R = alkyl; R1, R4 = H, Me; R2, R3 = H, alkyl; R2R3 = (CH2)m, CH2OCH2, CH2NHCH2; n = 1-3; m = 2,3; X = pharmaceutically-acceptable **anion**] were prepd. Thus, N-[2-[bis(1-methylethyl) **amino**]ethyl]-2-oxo-1-pyrrolidineacetamide was treated with MeI to give I (R-R4 = Me, X = iodo) (II). II, 5 mg/kg orally in mice, gave 87% reversal of **convulsive** electroshock-induced amnesia.

L7 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1983:48179 CAPLUS
DN 98:48179
TI Convulsant action of intracerebroventricularly administered L-kynurenine sulfate, quinolinic acid and other derivatives of succinic acid, and effects of amino acids: structure-activity relationships
AU Lapin, I. P.
CS Lab. Psychopharmacol., Bekhterev Psychoneurol. Res. Inst., Leningrad, USSR
SO Neuropharmacology (1982), 21(12), 1227-33
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB succinic acid [110-15-6] And the derivs. phthalic acid [88-99-3], L-glutamic acid [56-86-0], L-aspartic acid [56-84-8], citric acid [77-92-9], and levulinic acid [123-76-2] in doses of 5, 2, 5, 20, 20, and 50 .mu.g, resp., as well as L-kynurenine sulfate [16055-80-4] and quinolinic acid [89-00-9], injected into the brain ventricles in mice, induced clonic seizures. When administered i.p. or orally, they antagonize strychnine-induced seizures. The **convulsant** effect of L-kynurenine sulfate was obsd. only when the pH of the soln. was .ltoreq.4.0, while the actions of the other drugs tested were not dependent upon pH. Control intraventricular injections of 5 .mu.L of 0.06N H2SO4 (equiv. to 16.7 .mu.g SO42-, the same dose as was injected when a **convulsant** dose of 50 .mu.g L-kynurenine was administered) induced seizures in 25% of the mice. Thus, the **convulsant** effect of quinolinic acid and L-kynurenine sulfate is related to a moiety of succinic acid (O=C-C-C-C=O). The effect of L-kynurenine sulfate comprises the action of the cation of kynurenine and the **anion** of H2SO4. Redn. of the **convulsant** effect of L-kynurenine sulfate by .alpha.-**amino** acids and taurine [107-35-7] is presumably related to a shielding of the **amino**- and carbonyl groups of L-kynurenine. There is no evidence that L-kynurenine sulfate, in small doses, shares the central effects of the inhibitory **amino** acids.

L7 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1981:167377 CAPLUS
DN 94:167377
TI Barbiturate receptor sites are coupled to benzodiazepine receptors
AU Leeb-Lundberg, Fredrik; Snowman, Adele; Olsen, Richard W.
CS Dep. Biochem., Univ. California, Riverside, CA, 92521, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1980), 77(12), 7468-72
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Barbiturates enhanced the binding of 3H-labeled diazepam (I) [439-14-5] to benzodiazepine receptor sites in rat brain. Barbiturate enhancement of benzodiazepine binding was stereospecific, with the more anesthetic isomers of N1-methylbarbiturates being also more active than their stereoisomers in enhancing benzodiazepine binding. The active barbiturates produced a reversible enhancement in the affinity of specific benzodiazepine binding with no effect on the no. of binding sites. The barbiturate enhancement, but not the baseline benzodiazepine binding, was competitively inhibited by the **convulsant** picrotoxinin (1-10 .mu.M), a drug that has been shown to label barbiturate-sensitive brain membrane sites related to the .gamma.-**aminobutyric** acid receptor-ionophore complex. The barbiturate effect was also dependent upon the presence of certain **anions**, and only those **anions**, that penetrate the Cl- channels regulated by .gamma.-**aminobutyric** acid receptors. Apparently, picrotoxin-sensitive barbiturate binding sites were coupled to benzodiazepine receptors in the .gamma.-**aminobutyric** acid receptor-ionophore complex, and these binding sites had the properties of pharmacol. relevant receptors that mediate at least part of the action of various nervous system depressant and excitatory drugs.

L7 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1977:115640 CAPLUS
DN 86:115640
TI Structure-activity relations of excitatory amino acids on frog and rat spinal neurons
AU Biscoe, T. J.; Evans, R. H.; Headley, P. M.; Martin, M. R.; Watkins, J. C.
CS Med. Sch., Univ. Bristol, Bristol, UK
SO British Journal of Pharmacology (1976), 58(3), 373-82
CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
AB Compds. (0.25.mu.M-5mM) structurally related to glutamic acid [56-86-0] showed parallel structure-activity relations in their ability to depolarize the ventral roots of isolated hemisected frog spinal cord bathed in procaine (1mM) and to reduce the current (applied to single interneurons by microelectrophoresis) required to produce a given rate of neuronal firing in rat lumbar spine. Frog and rat spinal neurons must therefore have similar receptors for excitatory **amino** acids. Quisqualic acid (I) [52809-07-1], domoic acid [14277-97-5], and kainic acid [487-79-6] were the strongest excitants in both animals, with potencies approx. twice that of glutamate. 2,4,5-Trihydroxyphenylalanine (II) [21373-30-8] was a stronger excitant L-DOPA [59-92-7] a weaker excitant than glutamate on frog spinal motoneurons. II also was more potent **convulsant** than glutamate on intraventricular injection into mouse brain. Several of the compds. which are moderately active were not **anionic** at physiol. pH. Therefore, either 2 neg. charged groups are not essential for interaction with a common excitatory receptor or >1 type of receptor is involved.

L7 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1972:21669 CAPLUS
DN 76:21669
TI Toxicity of monosodium glutamate in young rats
AU Mushahwar, Isa K.; Koeppe, Roger E.
CS Agric. Exp. Stn., Oklahoma State Univ., Stillwater, OK, USA
SO Biochimica et Biophysica Acta (1971), 244(2), 318-21
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB The i.p. or intragastric injection of 5 mg Na L-glutamate (I) [142-47-2]/g to infant rats induced **convulsions** which were not due to ammonia [7664-41-7] but to **amino** acid **anions**. The **convulsions** were similar to those induced by Na L-aspartate [3792-50-5] and Na D-glutamate [15383-53-6]. I increased the brain glutamine [56-85-9], but not glutamate [56-86-0]. Glycine [56-40-6] did not cause **convulsions**, but did elevate brain glutamine.

L7 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1971:109939 CAPLUS
DN 74:109939
TI Thiosemicarbazide and .gamma.-aminobutyric acid metabolism
AU Sze, Paul Y.; Kuriyama, Kinya; Roberts, Eugene
CS Div. Neurosci., City Hope Natl. Med. Cent., Duarte, CA, USA
SO Brain Research (1971), 25(2), 387-96
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB The retention of endogenous .gamma.-**aminobutyric** acid (I) and the accumulation of exogenously added 14C-labeled I or glutamate by mouse brain synaptosomes, mitochondria, and synaptic vesicles at 0.degree. were not significantly affected in vitro by 5 .times. 10-4-10-2M thiosemicarbazide (II). Prior i.p. injection of 50 mg II/kg into mice pretreated with **aminooxyacetic** acid to block I metabolism via transamination did not alter from the controls the distribution of radioactivity of 3H-labeled I. Treatment with II did not increase the penetrability of I into the brain. II treatment did not alter the amt. of retention in brain or the rate of appearance of radioactivity in liver, kidney, urine, and blood at 45 min after intraventricular administration of 3H-labeled I to control and II-injected rabbits that had previously been injected with **aminooxyacetic** acid. Electropherograms prepd. from exts. of brain showed the radioactivity in the brains of the controls to be entirely assocd. with I; however, exts. from brains of II-treated rabbits contained an unidentified **anionic** substance in addn. to I. This substance was also found in liver exts. of II-treated, but not untreated, animals. The direct action of II that results in **convulsions** in animals may be on nonneural elements in the brain or the direct effect on neurons may be a deriv. of II, not II itself.

L7 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2003 ACS
AN 1956:77976 CAPLUS
DN 50:77976
OREF 50:14804a-i,14805a-c
TI Steroidal amines. III. 16.alpha.-Amino-substituted pregnanes
AU Gould, David; Shapiro, Elliot L.; Finckenor, Lawrence E.; Gruen, Fred; Hershberg, E. B.
CS Schering Corp., Bloomfield, NJ
SO J. Am. Chem. Soc. (1956), 78, 3158-63
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA Unavailable
AB cf. C.A. 50, 8700i. 5,16-Pregnadien-3.beta.-ol-20-one (I) and the acetate (II) of I gave with unhindered primary and secondary **amines** in the presence of a basic catalyst, such as an aq. base or an **anion** exchange resin in the hydroxide form, substituted 16.alpha.-**amino**-5-pregnen-3.beta.-ol-20-ones (III). II (1 g.) dissolved by warming in 4 cc. piperidine, treated with 0.25 g. 86% KOH in 0.3 cc. H2O, stirred 2 hrs. on the steam bath and then at room temp. overnight, poured with stirring into 400 cc. H2O, allowed to stand 1 hr., and filtered yielded 1.15 g. 16.alpha.-piperidino-5-pregnen-3.beta.-ol-20-one (IV), needles, m. 131-5.degree.; the crude IV recrystd. from C6H6 gave C6H6-solvated IV, m. 149-51.degree., [.alpha.]D25 -20.0.degree. (all rotations are in dioxane unless otherwise stated), which dried 6 hrs. at 1 mm. over PhMe gave IV, m. 149-51.degree. with slight sintering at 131-8.degree., [.alpha.]D25 -23.5.degree., [.alpha.]D25 .+-. 0.degree. (EtOH). IV treated with concd. HCl gave IV.HCl, m. 240-2.degree. (from MeOH-Me2CO) (decompn.), [.alpha.]D25 8.7.degree.. In 1 instance crystn. from C6H6 gave a different, possibly not solvated form, m. 160-2.degree., [.alpha.]D25 -24.7.degree.. Similarly were prepd. the following III (16-substituent, m.p., and [.alpha.]D25 given): MeNH, 166.5-7.5.degree. (from Me2CO), -22.6.degree.; EtNH crystg. with 1 mole Me2CO, 113.4-15.4.degree. (from Me2CO), -23.2.degree.; PrNH (V), 85-8.degree. (from C6H6-hexane), -21.8.degree.; V.C6H6, 84-7.5.degree. (from C6H6), -19.9.degree. [-0.1 (EtOH), -14.8.degree. (CHCl3)]; iso-PrNH, 133-5.degree. (from Me2CO-hexane), -26.4.degree.; CH2:CHCH2.HCl, 247-8.5.degree. (decompn.) (from MeOH-Me2CO), 10.5.degree.; BuNH, 106-8.degree. (from C6H6), -25.degree.; iso-BuNH, 108-10.degree. (from C6H6), -27.6.vkappa.; EtMeCHNH, 120-2.degree. (from C6H6-hexane), -32.2 .degree.; AmNH, 124.5-6.0.degree. (from C6H6-hexane), -20.6.degree.; iso-AmNH, 130-3.degree. (from C6H6-hexane), -23.6.degree.; C6H13NH, 111.4-12.6.degree. (from Me2CO), -23.3.degree.; iso-C6H13NH (VI), 124-6.degree. (from Me2CO), -18.1.degree.; VI.HCl, 251-2.degree. (decompn.) (from MeOH-Me2CO), 9.3.degree.; BuEtCHCH2NH, 102.5-5.0.degree. (from C6H6-hexane), -20.6.degree.; PhCH2NH, 148-50.degree. (from C6H6-Me2CO), -38.8.degree.; Me2N, 204-5.5.degree. (from C6H6) -19.degree.; pyrrolidino, 145-7.degree. (from C6H6 and EtOAc), -17.6.degree.; morpholino, 180-1.degree. (from C6H6), -11.8.degree.. IV (5 g.) in 20 cc. dry pyridine treated with 10 cc. Ac2O, kept 2 hrs. at room temp., poured into H2O, basified, and filtered yielded the 3-acetate of IV, m. 176-8.degree. (from EtOH), [.alpha.]D25 -22.degree.. IV treated 8 hrs. in the same manner with 1 part iso-PrCOCl in 10 vols. pyridine gave the 3-isobutyrate, m. 140-1.degree., [.alpha.]D25 -12.6.degree.. IV gave similarly with veratroyl chloride heated 4 hrs. at 45-53.degree. and stirred at room temp. overnight 3-veratrate of IV, m. 154-5.5.degree., [.alpha.]D25 18.6.degree.. IV (5 g.) in 25 cc. Ac2O refluxed 2.5 hrs., treated with Darco G-60, filtered, and chilled gave 2.54 g. acetate (V) of 5,16-pregnadien-3.beta.-ol-20-one acetate, m. 176.2-7.2.degree. (from

iso-PrOH). IV (5 g.) in 25 cc. dry pyridine refluxed 20 hrs. with 3 g. iso-PrCOCl and evapd. to dryness in vacuo, and the residue worked up with C6H6 yielded 4.5 g. isobutyrate of V, m. 164-5.degree. (from MeOH), [.alpha.]D25 -39.1.degree.. 16.alpha.-PhCH2NH analog of IV (4 g.) in 25 cc. C6H6 and 8 cc. MeOH treated with 8 g. MeI and refluxed 1 hr., treated with 0.4 g. NaOH and 8 g. MeI, refluxed 1 hr., kept at room temp. overnight, and filtered, the filtrate evapd., and the residue digested with Et2O gave 4.5 g. 16.alpha.-(N,N-dimethylbenzylammonium)-5-pregnen-3.beta.-ol-20-one iodide, m. 228-30.degree. (decompn.) (from Me2CO-MeOH and MeOH). IV (4 g.) in 25 cc. C6H6 and 8 cc. MeOH refluxed 1 hr. with 3.5 cc. MeI and cooled gave 3.55 g. IV.MeI, m. 271.5-2.5.degree. (decompn.) (from MeOH-C6H6), [.alpha.]D25 18.4.degree. (95% EtOH). IV (2 g.) in 50 cc. glacial AcOH treated with 1.5 g. 10% Pd-C, shaken with H at 1 atm. and 25.degree., filtered, and poured into 1 l. 10% aq. Na2CO3 yielded 1.95 g. 16.alpha.-piperidinoallopregnan-3.beta.-ol-20-one (VIa), m. 169.5-70.5.degree. (from EtOH), [.alpha.]D25 49.6.degree. (95% EtOH). IV (4 g.) in 50 cc. MeOH contg. 2 cc. H2O and 4 g. NaBH4 in 30 cc. MeOH heated to boiling, and the soln. kept at room temp. overnight and poured into 400 cc. H2O gave 3.3 g. 16.alpha.-piperidino-5-pregnene-3.beta.,20-diol (VII), m. 184-6.degree. (from EtOH and MeOH), [.alpha.]D25 -97.6.degree.; VII.HCl, m. 292.5-93.degree. (decompn.), [.alpha.]D25 -43.7.degree.; the mother liquor gave fractions with lower rotations. VII refluxed with MeI gave VII.MeI, m. 299 300.degree. (decompn.) (from Me2CO-MeOH and MeOH). VII (24 g.) in 100 cc. AcOH hydrogenated 1 hr. over 2 g. PtO2, filtered, and poured into 2 l. H2O contg. 250 g. KOH, the ppt. refluxed in 700 cc. MeOH with 12 g. KOH in 50 cc. H2O for 1.5 hrs., the soln. concd., the residue treated with 2 l. H2O, dried at 60.degree. 3 hrs. in vacuo and then overnight in vacuo, and dissolved in C6H6, the aq. layer removed, and the C6H6 layer concd. to 150 cc. and allowed to stand gave 18.5 g. 16.alpha.-piperidinoallopregnane-3.beta.,20-diol (VIII) (probably 20.beta.), m. 178-80.degree. (from C6H6), [.alpha.]D25 -55.2.degree.; the mother liquor concd., gave a 2nd form (possibly 20.alpha.), m. 185-90.degree., [.alpha.]D25 -57.0.degree.; VIII.MeI, m. 286-8.degree. (from MeOH). The following derivs. of 16.alpha.-piperidino-.DELTA.5-allopregnene-3.beta.-ol-20-one (IX) [lower-melting form, m. 149-51.degree. (from MeOH-C6H6), [.alpha.]D25 -23-5.degree.; higher-melting form, m. 160-2.degree., [.alpha.]D25 -24.7.degree.] were prepd. (m.p. and [.alpha.]D25 given): HCl salt 240-2.degree. (decompn.) (from MeOH-Me2CO), 8.7.degree.; H maleate, 203-5.degree. (decompn.) (from MeOH), 8.4.degree.; H tartrate, 166.degree. [resolidified at 175.degree. and remelted at 203-5.degree. (decompn.)] (from EtOH), 17.1.degree. [15.4.degree. (H2O)]; 3-isobutyrate HCl salt, 238.degree. (decompn.) (from C6H6), 0.degree.; 3-veratrate HCl salt, 243.5-4.5.degree. (decompn.) (from C6H6), 24.6.degree.; 3'-Me deriv. (X), 172-5.degree. (from C6H6-hexane), -23.2.degree.; X.HCl (lower-melting form), 215-17.5.degree. (decompn.) (from MeOH-Me2CO), 16.7.degree.; X.HCl (higher-melting form), 222-6.5 (decompn.) (from MeOH-Me2CO), 8.8.degree.; 4'-Me, 168-70.degree. (from C6H6), -23.8.degree.. The III stimulate the central nervous system to cause severe **convulsions** in nonanesthetized dogs at antiaccelerator doses.

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=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2026 OR  2039 OR  2047 OR  2045

L8    SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\09932677 (af).str

L9      STRUCTURE UPLOADED

=> que L9 NOT L8

L10  QUE L9 NOT L8

=> d l10
L10 HAS NO ANSWERS
L8              SCR 2026 OR 2039 OR 2047 OR 2045
L9              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L10             QUE  L9 NOT L8


=> s l10 sss sam
SAMPLE SEARCH INITIATED 16:15:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  47572 TO ITERATE

  2.1% PROCESSED    1000 ITERATIONS                                  50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       938484 TO   964396
PROJECTED ANSWERS:          393042 TO   409972

L11          50 SEA SSS SAM L9 NOT L8

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ENTER SCREEN EXPRESSION OR (END):end


=> screen 1835

L12   SCREEN CREATED

=> screen 2026 OR  2039 OR  2047 OR  2045

L13   SCREEN CREATED

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Uploading C:\STNEXP4\QUERIES\09932677 (af).str

L14     STRUCTURE UPLOADED

=> que L14 AND L12 NOT L13

L15  QUE L14 AND L12 NOT L13

=> d l15
L15 HAS NO ANSWERS
L12             SCR 1835
L13             SCR 2026 OR 2039 OR 2047 OR 2045
L14             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L15             QUE  L14 AND L12 NOT L13


=> s l15 sss sam
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SAMPLE SCREEN SEARCH COMPLETED -   9923 TO ITERATE

 10.1% PROCESSED    1000 ITERATIONS                                  50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       192496 TO   204424
PROJECTED ANSWERS:           91707 TO   100005

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=> s l15 sss ful
FULL SEARCH INITIATED 16:18:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 198359 TO ITERATE

100.0% PROCESSED  198359 ITERATIONS                             96597 ANSWERS
SEARCH TIME: 00.00.08

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=> s l17
L18      58526 L17

=> s l3 and l18
L19        130 L3 AND L18

=> s l6 and l18
L20        281 L6 AND L18

=> s l19 or l20
L21        376 L19 OR L20

=> s epileptogen?
L22       1844 EPILEPTOGEN?
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=> s l22 and l18
L23          34 L22 AND L18

=> d l23 1-34 bib,ab,hitstr
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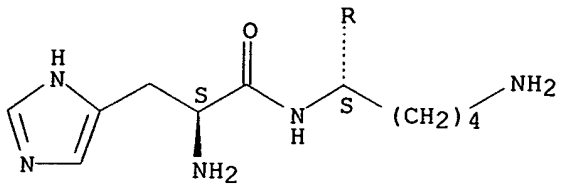
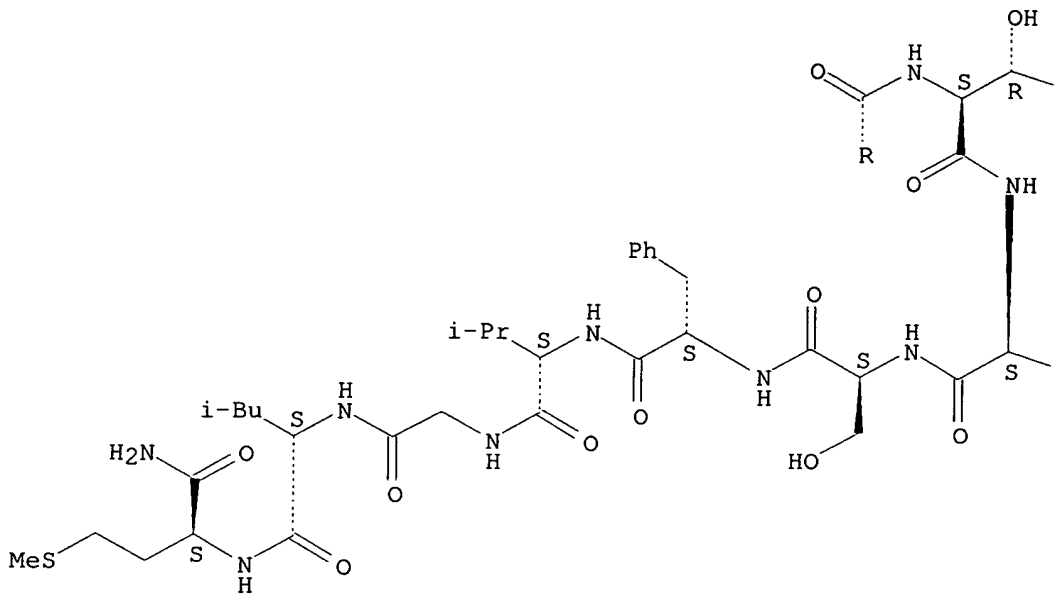
L23 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 2002:838562 CAPLUS
DN 138:181215
TI Activation of neurokinin-1 receptors promotes GABA release at synapses in the rat entorhinal cortex
AU Stacey, A. E.; Woodhall, G. L.; Jones, R. S. G.
CS School of Medical Sciences, Department of Physiology and MRC Centre for Synaptic Plasticity, University of Bristol, Bristol, BS8 1TD, UK
SO Neuroscience (Oxford, United Kingdom) (2002), 115(2), 575-586
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
AB We have previously shown that activation of neurokinin-1 receptors reduces acutely provoked epileptiform activity in rat entorhinal cortex in vitro, and suggested that this may result from an increase in GABA release from inhibitory interneurons. In the present study we have made whole cell patch clamp recordings of spontaneous GABA-mediated inhibitory postsynaptic currents as an indicator of GABA release in slices of rat entorhinal cortex, and detd. the effects of neurokinin receptor activation on this release. The neurokinin-1 receptor agonists septide and GR 73632 provoked a robust increase in the frequency of GABA-mediated currents, and an increase in mean amplitude. The effects were mimicked by substance P, and blocked by a neurokinin-1 receptor antagonist. High concns. of neurokinin A had similar effects, which were also blocked by the neurokinin-1 receptor antagonist, but agonists at neurokinin-2 or neurokinin-3 receptors were ineffective. The increases in amplitude and frequency of events provoked by septide were prevented by prior blockade of action potential-dependent release with tetrodotoxin. In current clamp recordings from putative interneurons, GR 73632 evoked depolarization and a prolonged discharge of action potentials. Finally, recordings from pyramidal neurons and oriens-alveus interneurons in CA1 of the hippocampus showed that application of GR 73632 caused an increase in frequency and amplitude of GABA-mediated inhibitory postsynaptic currents in the former and persistent firing of action potentials in the latter. The results demonstrate that neurokinin-1 receptor activation promotes the release of GABA at synapses on principal neurons in both entorhinal cortex and hippocampus. The abolition of this effect by tetrodotoxin and the excitatory responses seen in interneurons clearly suggest that the neurokinin-1 receptor is localized on the soma-dendritic domain of the inhibitory neurons. Thus, substance P inputs to inhibitory neurons may have a widespread influence on cortical network excitability and could play a role in **epileptogenesis** and its control.
IT **86933-74-6**, Neurokinin A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neurokinin-1 receptor activation promotion of GABA release at synapses in rat entorhinal cortex and hippocampus)
RN 86933-74-6 CAPLUS
CN Neurokinin A (swine spinal cord) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

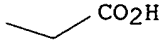
PAGE 1-A



PAGE 2-A



PAGE 2-B



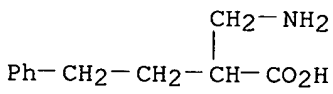
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD

L23 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 2002:716608 CAPLUS
DN 137:242191
TI Antiepileptogenic agents
IN Weaver, Donald F.; Tan, Christopher Y. K.; Kim, Stephen T.; Kong, Xianqi; Wei, Lan; Carran, John R.
PA Queen's University at Kingston, Can.; Neurochem Inc.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002073208	A2	20020919	WO 2002-CA363	20020313

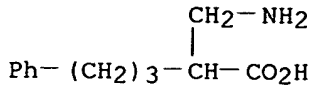
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-275618P P 20010313
OS MARPAT 137:242191
AB The invention discloses methods and compds. useful for the treatment of convulsive disorders, including epilepsy. The methods and compds. of the invention inhibit or prevent ictogenesis and/or **epileptogenesis**. The invention also discloses methods for prepg. these anticonvulsant compds.
IT **460039-38-7 460039-39-8 460039-44-5 460039-45-6**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**epileptogenic** agents)
RN 460039-38-7 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

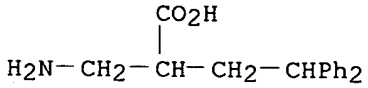


● HCl

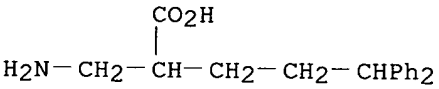
RN 460039-39-8 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 460039-44-5 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-.gamma.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

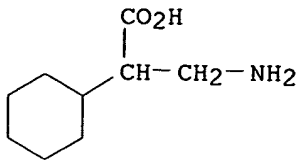


RN 460039-45-6 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-.delta.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

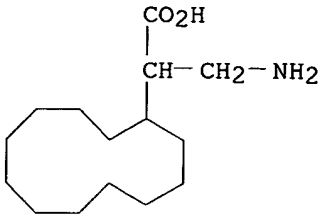


IT **107-95-9D**, .beta.-Alanine, esters
RL: PAC (Pharmacological activity); BIOL (Biological study)
(anti-**epileptogenic** agents)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

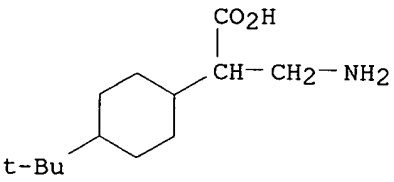
IT **5664-30-2P 213192-16-6P 213192-49-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-**epileptogenic** agents)
RN 5664-30-2 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)

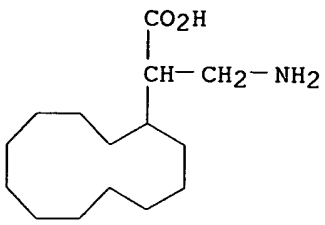


RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **213192-76-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(anti-**epileptogenic** agents)
RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

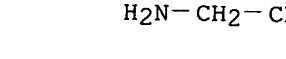
L23 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1998:621100 CAPLUS
DN 129:239901
TI Anti-**epileptogenic** agents, and preparation thereof
IN Weaver, Donald F.; Milne, Paul H.; Tan, Christopher Y. K.; Carran, John R.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English

Applicant's

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840055	A2	19980917	WO 1998-CA244	19980312
	WO 9840055	A3	19990218		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6306909	B1	20011023	US 1998-41371	19980311
	AU 9864923	A1	19980929	AU 1998-64923	19980312
	EP 969823	A2	20000112	EP 1998-910555	19980312
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 337849	A	20000128	NZ 1998-337849	19980312
	JP 2001515483	T2	20010918	JP 1998-539010	19980312
	US 2002025949	A1	20020228	US 2001-932676	20010816
PRAI	US 1997-41140P	P	19970312		
	US 1998-73536P	P	19980203		
	US 1998-41371	A3	19980311		
	WO 1998-CA244	W	19980312		

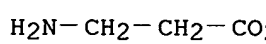
OS MARPAT 129:239901
AB Methods and compds. useful for the inhibition of convulsive disorders, including epilepsy, are disclosed. The methods and compds. of the invention inhibit or prevent ictogenesis and **epileptogenesis**. Methods for prepg. the compds. of the invention are also described.
IT **107-95-9**, .beta.-Alanine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anti-**epileptogenic** agents for convulsive disorder treatment, and prepn. thereof)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



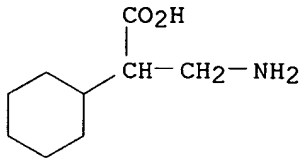
IT **107-95-9DP**, .beta.-Alanine, derivs. **5664-30-2P 213192-48-4P 213192-49-5P 213192-50-8P 213192-76-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anti-**epileptogenic** agents for convulsive disorder treatment, and prepn. thereof)

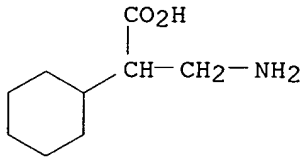
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 5664-30-2 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)

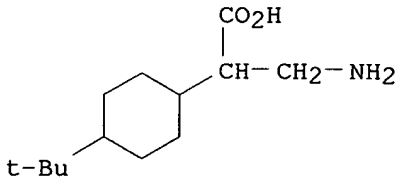


RN 213192-48-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

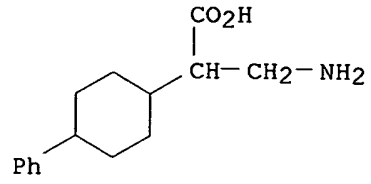
RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

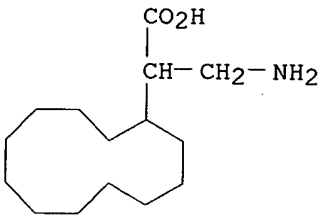
RN 213192-50-8 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl-, hydrochloride

(9CI) (CA INDEX NAME)



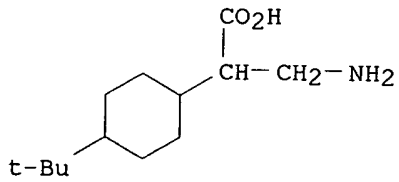
● HCl

RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

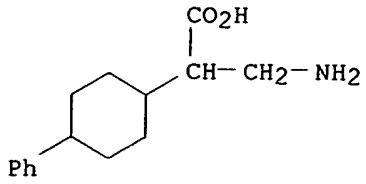


● HCl

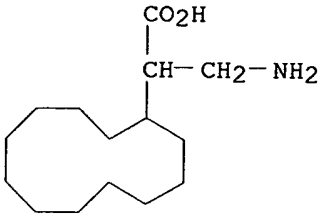
IT **213192-14-4 213192-15-5 213192-16-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**epileptogenic** agents for convulsive disorder treatment, and prepn. thereof)
RN 213192-14-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



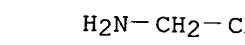
RN 213192-15-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl- (9CI) (CA INDEX NAME)



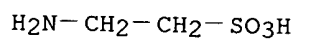
RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)



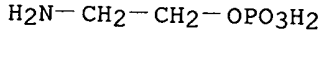
L23 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1997:586697 CAPLUS
DN 127:276503
TI Increased excitatory amino acid levels in brain cysts of epileptic patients
AU Hajek, Marketa; Do, Kim Quang; Duc, Corinne; Boesiger, Peter; Wieser, Heinz Gregor
CS Neurology Department, University Hospital Zuerich, Frauenklinikstr. 26, Zurich, CH-8091, Switz.
SO Epilepsy Research (1997), 28(3), 245-254
CODEN: EPIRE8; ISSN: 0920-1211
PB Elsevier
DT Journal
LA English
AB The authors studied two epileptic patients with arachnoid brain cysts by proton magnetic resonance spectroscopy (1H MRS). In addn., histochem. analyses of surgical specimens, cerebrospinal fluid, and cystic fluid were performed in one of the patients. In both patients, greatly increased levels of excitatory amino acids (EAAs) glutamate and aspartate were present in the cystic fluid, while there was only a moderate increase of glutamate in the **epileptogenic** brain tissue adjacent to the cyst in one of the patients. In non-epileptic brain regions, no elevations of the EAAs were present. Since EAAs are involved in induction and maintenance of **epileptogenesis**, their extremely high concns. in the cystic fluid may explain seizures in some patients with such brain cysts. The authors' findings may have therapeutical consequences for patients with drug resistant epilepsy, in whom elevated concns. of EAAs in the cysts can be verified. Surgery with the aim to create a communication between the cyst and the subarachnoidal space may prevent an accumulation of the EAAs and thus result in a relief of seizures.
IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(amino acids and derivs. in arachnoid brain cyst, cisternal cerebrospinal fluid, and ganglioglioma of human with epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1993:252606 CAPLUS
DN 118:252606
TI Co-variation of free amino acids in human **epileptogenic** cortex
AU Hamberger, Anders; Haglid, Kenneth; Nystroem, Britta; Silfvenius, Herbert
CS Inst. Neurobiol., Univ. Goeteborg, Swed.
SO Neurochemical Research (1993), 18(4), 519-25
CODEN: NEREDZ; ISSN: 0364-3190
DT Journal
LA English
AB The concn. of free amino acids was measured in 41 surgically removed samples of human **epileptogenic** brain and in 7 specimens of non-epileptic brain tissue, removed during surgery for meningiomas, etc. The material was subdivided according to the neuropathol. diagnosis: mild cortical dysplasia (MCD), gliosis astrocytoma infiltration and a histol. heterogeneous group. The non-tumoral **epileptogenic** samples had five times higher than normal concn. of ethanolamine and 50% elevated concn. of glycine. The concn. of other neurotransmitter amino acids did not differ markedly between **epileptogenic** and non-epileptic samples. The concn. of neurotransmitter amino acids showed a strong correlation with the enzyme neuron-specific enolase (NSE) and were low in most samples with astrocytoma infiltration. On the other hand, tyrosine and leucine had higher concns. in samples with lower NSE concn. Factor anal. of the amino acids revealed four groups of co-varying compds. in the brain samples, first, a neurotransmitter group, including aspartate, glutamate, GABA and phosphoethanolamine. Another group contained ethanolamine, glutamine, glycine and taurine. Factor anal. on corresponding extracellular amino acids showed two groups, the first being a "neurotransmitter" group, contg. serine, taurine phosphoethanolamine and ethanolamine in addn. to aspartate and glutamate. The other group consisted of asparagine, glycine, alanine, tyrosine, valine, phenylalanine, isoleucine and leucine.
IT **107-35-7**, Taurine **1071-23-4**, Phosphoethanolamine
RL: BIOL (Biological study)
(of brain, of human, in epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



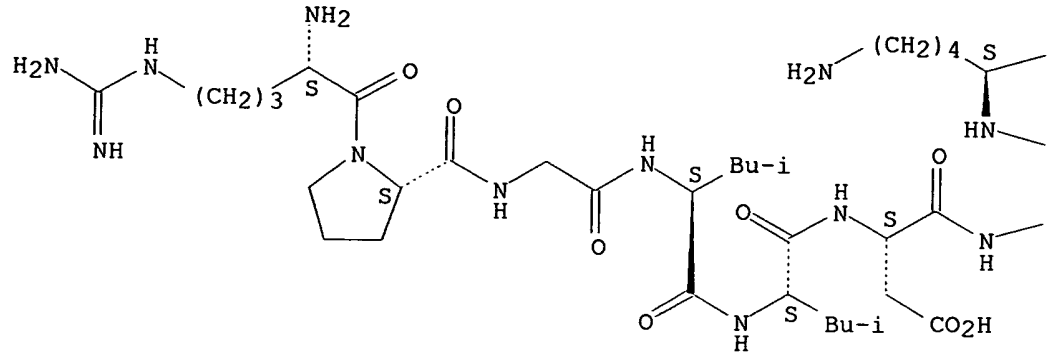
RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)



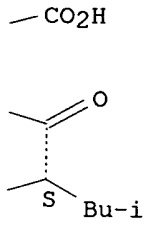
L23 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1992:445867 CAPLUS
DN 117:45867
TI **Epileptogenic** activity of two peptides derived from diazepam-binding inhibitor after intrahippocampal injection in rats
AU Vezzani, A.; Serafini, R.; Stasi, M. A.; Samanin, R.; Ferrarese, C.
CS Ist. Ric. Farmacol. "Mario Negri", Milan, 20157, Italy
SO Epilepsia (1991), 32(5), 597-603
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB Peptides DBI 42-50 (DRPGLLDLK) and DBI 43-50 (RPGLLDLK) are synthetic fragments of an 18-amino acid peptide called octadecaneuropeptide (QATVGDVNTDRPGLLDLK), a brain deriv. of diazepam-binding inhibitor (DBI). The two peptides were unilaterally injected into the dorsal hippocampus (granule cells of dentate gyrus) of freely moving adult rats. The EEG pattern was continuously recorded from bilateral hippocampal and cortical electrodes, and the animals' behavior was obsd. throughout the expt. A dose of 100 nmol peptide 42-50 was required to cause reliably EEG alterations (seizures and spiking). EEG changes, defined as seizures, were characterized by discrete repetitive periods of high-frequency and(or) multispike complexes and(or) high-voltage synchronized spike or wave activity. EEG seizures were often assocd. with a frozen appearance of the animal and wet dog shakes. Tonic-clonic convulsions were not obsd. EEG seizures induced by peptide 42-50 were prevented by 90 mg/kg PK 11195, a selective antagonist of a novel GABAA receptor-linked subtype of a benzodiazepine (BDZ) receptor, but were unaffected by flumazenil, an agonist of the central type of BDZ receptor and by D(-)2-amino-7-phosphonoheptanoic acid, a selective antagonist of the N-methyl-D-aspartate subtype of excitatory amino acid receptors. Light microscopy showed no neuropathol. changes in the injected hippocampus. Thus, these DBI-derived peptide fragments induce a typical pattern of limbic seizures in rats. DBI and(or) its natural processing products may play a role in the pathophysiol. of epilepsy.
IT **101510-85-4 120550-29-0**
RL: BIOL (Biological study)
(brain elec. activity changes and seizure activity induced by, epilepsy pathogenesis in relation to)
RN 101510-85-4 CAPLUS
CN L-Lysine, L-arginyl-L-prolylglycyl-L-leucyl-L-leucyl-L-.alpha.-aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



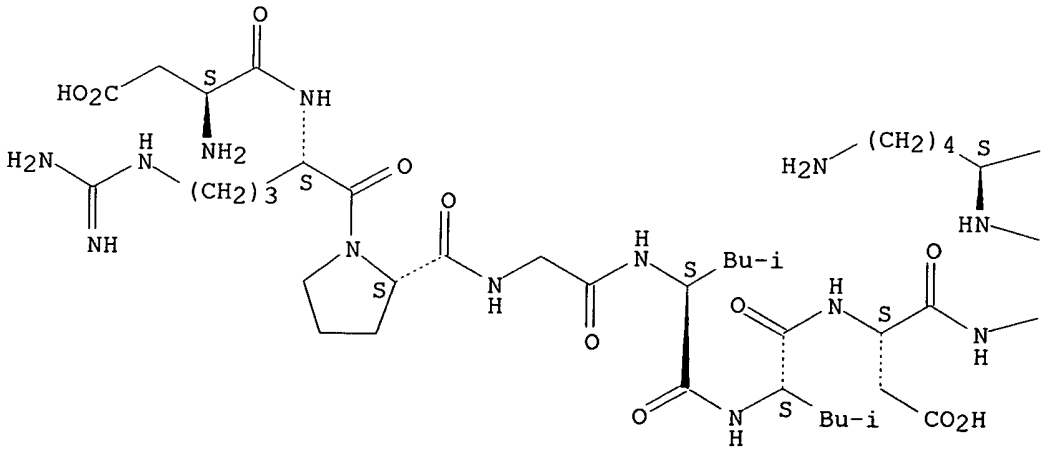
PAGE 1-B



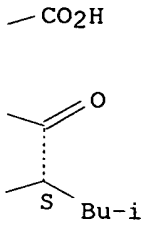
RN 120550-29-0 CAPLUS
CN L-Lysine, N2-[N-[N-[N-[N-[1-(N2-L-.alpha.-aspartyl-L-arginyl)-L-prolyl]glycyl]-L-leucyl]-L-leucyl]-L-.alpha.-aspartyl]-L-leucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

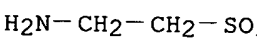
PAGE 1-A



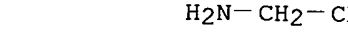
PAGE 1-B



L23 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1992:126155 CAPLUS
DN 116:126155
TI Amino-acid analysis in **epileptogenic** foci
AU Wang, Yifang; Tan, Gifu
CS Dep. Brain Surg., Nanjing Mil. Gen. Hosp., Nanjing, Peop. Rep. China
SO Jiangsu Yiyao (1991), 17(11), 585-7
CODEN: CIYADX; ISSN: 0253-3685
DT Journal
LA Chinese
AB The amino acids glycine, arginine, tyrosine, glutamine, and aspartic acid were increased in **epileptogenic** foci (e.g. hippocampus and amygdaloid nucleus) removed from epileptic patients.
IT **107-35-7**, Taurine
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in brain **epileptogenic** foci of humans with epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1990:435225 CAPLUS
DN 113:35225
TI The **epileptogenic** action of the taurine analog guanidinoethane sulfonate may be caused by a blockade of GABA receptors
AU Herranz, A. S.; Solis, J. M.; Herreras, O.; Menendez, N.; Ambrosio, E.; Orensanz, L. M.; Martin del Rio, R.
CS Dep. de Invest., Hosp. Ramon y Cajal, Madrid, 28034, Spain
SO Journal of Neuroscience Research (1990), 26(1), 98-104
CODEN: JNREDK; ISSN: 0360-4012
DT Journal
LA English
AB To clarify the mechanism through which the taurine analog guanidinoethane sulfonate (GES) produces its **epileptogenic** effects, in vivo expts. were performed in the rat hippocampus with a brain dialysis probe that also contained a recording electrode. Perfusion of 10 mM GES induced an enhancement of extracellular taurine levels, probably as a result of forced efflux through the taurine uptake systems in a heteroexchange process. This taurine increase was highly reversible. GES also induced an increase of neuronal excitability and an impairment of recurrent inhibition as judged by the neuronal pattern discharge of evoked potentials. These results indicated the possible implication of GABA receptors in the **epileptogenic** effect of GES. Specific binding of [3H]GABA to synaptosomal-mitochondrial (P2) fractions was inhibited by both bicuculline methiodide (BMI) and GES with the same potency. Similar results were obtained using cerebral sections. Autoradiog. expts. confirmed the binding results, with GES and BMI completely displacing [3H]GABA binding. Apparently, the **epileptogenic** GES action is due to a direct antagonism on GABAA receptors, rather than to a decrease in endogeneous taurine content.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain extracellular spaces, guanidinoethane sulfonate effect on, **epileptogenic** activity in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



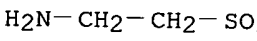
L23 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1988:605524 CAPLUS
DN 109:205524
TI Glycine potentiates strychnine-induced convulsions: role of NMDA receptors
AU Larson, Alice A.; Beitz, Alvin, J.
CS Dep. Vet. Biol., Univ. Minnesota, St. Paul, MN, 55108, USA
SO Journal of Neuroscience (1988), 8(10), 3822-6
CODEN: JNRSDS; ISSN: 0270-6474
DT Journal
LA English
AB Strychnine poisoning leads to seizures that have been attributed to competitive antagonism of glycine receptors in the spinal cord. Although glycine is thought to act as an inhibitory neurotransmitter, a strychnine-insensitive glycine receptor (Gly2) has been described in cultured mouse neurons that is thought to be allosterically linked to the excitatory amino acid N-methyl-D-aspartate (NMDA) receptor. Intrathecally administered glycine, in contrast to other putative inhibitory transmitters, potentiated rather than inhibited strychnine-induced convulsions in mice. The seizure-potentiating effects of glycine were blocked by aminophosphonovaleric acid, an NMDA antagonist. In animals pretreated with a subconvulsive dose of strychnine to block strychnine-sensitive glycine receptors (Gly1), glycine enhanced, rather than inhibited, NMDA-induced convulsions. Thus, the seizure-potentiating effects of glycine apparently involve activation of NMDA receptors. This provides the 1st evidence that glycine is capable of modulating the activity of NMDA receptors in the spinal cords of adult animals. In light of the elevated concns. of glycine found in **epileptogenic** brain foci, glycine may be a pos. modulator in the prodn. of epileptic seizures.
IT **107-35-7**, Taurine **107-95-9**, .beta.-Alanine
RL: BIOL (Biological study)
(convulsions from strychnine inhibition by)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

L23 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1987:595933 CAPLUS
DN 107:195933
TI Amino acids, 5-hydroxytryptamine, and catecholamines in iron-induced **epileptogenic** foci of the rat
AU Hiramatsu, Midori; Fukushima, Masato; Kabuto, Hideaki; Edamatsu, Rei; Mori, Akitane
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Advances in Epileptology (1987), Volume Date 1985, 16th, 151-4
CODEN: ADEPDN; ISSN: 0892-726X
DT Journal
LA English
AB An **epileptogenic** focus was induced by injection of FeCl3 into the cerebral cortex of rats. The serotonin level in the pons-medulla increased 15 min after the injection. The serotonin level in the midbrain increased, that in the cortex decreased at 30 min, and that in the cerebellum increased 2 mo after the injection. The dopamine and norepinephrine levels in the brain regions were not affected by the FeCl3 injection. Amino acids levels in the ipsilateral cerebral cortex also were not affected at 2 mo after the FeCl3 injection, whereas the valine level in the cerebellum decreased. Serotonin might play a role in the Fe-induced epileptic seizure mechanism, whereas catecholamines and amino acid neurotransmitters are probably not involved.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain areas, in epilepsy induced by cerebral iron injection)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1986:550890 CAPLUS
DN 105:150890
TI Focal **epileptogenesis**: a role for taurine?
AU Golden, G. T.; Fariello, R. G.; Ente, P.
CS VAMC, Coatesville, PA, 19320, USA
SO Neurotransm., Seizures, Epilepsy 3, [Workshop], 3rd (1986), Meeting Date 1985, 179-87. Editor(s): Nistico, Giuseppe. Publisher: Raven, New York, N. Y.
CODEN: 55FWAL
DT Conference
LA English
AB Application of aq. solns. .gtoreq.25 mM of TAG [an inhibitor of taurine (TAU)] to the cerebral cortex of adult, urethane-anesthetized rats induced transient **epileptogenic** discharges. Aq. solns. .gtoreq.50 mM consistently induced electrog. single epileptic spikes within 2 min, and these spikes continued up to 70 min. Epileptiform activity was suppressed by equimolar solns. of GABA. Topically applied equimolar solns. of TAU potentiated spike activity; glycine and .beta.-alanine had no effect in general. Thus, the hypothesis of a direct involvement of TAU in cortical focal **epileptogenesis** is not supported.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, in focal epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

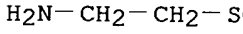
IT **107-95-9**
RL: BIOL (Biological study)
(taurine-induced focal epilepsy response to)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

L23 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1986:550871 CAPLUS
DN 105:150871
TI Electroencephalographic effects of centrally administered phosphoethanolamine and glutamic acid
AU Lehmann, A.; Laird, H. E.; Huxtable, R. J.
CS Coll. Med., Univ. Arizona, Tucson, AZ, 85724, USA
SO Proceedings of the Western Pharmacology Society (1986), 29, 227-31
CODEN: PWPSA8; ISSN: 0083-8969
DT Journal
LA English
AB Intracerebroventricular injections of phosphoethanolamine (PEA) into rats produced dose-dependent epileptiform activity as assessed by EEG and behavioral changes. The potency of PEA was roughly comparable to that of glutamate. The role of PEA in **epileptogenesis** is discussed.
IT **1071-23-4**
RL: BIOL (Biological study)
(brain function response to, epilepsy in relation to)
RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-OPO_3H_2$

L23 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1986:531578 CAPLUS
DN 105:131578
TI The **epileptogenic** action of 6-aminomethyl-3-methyl-1-4H-1,2,6-benzothiadizine-1,1-dioxide hydrochloride (TAG): non-specific versus specific antitaurine pathogenesis
AU Fariello, Ruggero G.; Golden, Gregory T.; Ente, Philip
CS Res. Neurol. Serv., VA Med. Cent., Coatesville, PA, 19320, USA
SO Brain Research (1986), 380(1), 196-200
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Cortical superfusion with 6-aminomethyl-3-Me-1-4H-1,2,6-benzothiadiazine-1,1-dioxide hydrochloride (TAG) at a concn. which selectively blocks taurine (Tau) action fails to modify EEG activity, cortical neuronal firing, and caudate-induced inhibition of cortical neuronal activity. Higher concns. of TAG increase neuronal firing rate and eventually induce EEG interictal spikes that can be suppressed by topical GABA but not by glycine or .beta.-alanine. Topical Tau consistently enhances the epileptiform activity. Apparently, specific blockade of Tau does not affect any of the physiol. function under observation and the **epileptogenic** effect of TAG is due to its GABA antagonist action.
IT **107-35-7**
RL: BIOL (Biological study)
(in epilepsy from TAG, GABA in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1986:477016 CAPLUS
DN 105:77016
TI Effect of altered blood plasma osmolalities on regional brain amino acid concentrations and focal seizure susceptibility in the rat
AU Baxter, Claude F.; Wasterlain, Claude G.; Hallden, Kristine L.; Pruess, Sharon F.
CS Epilepsy Res. Lab., VA Medical Cent., Sepulveda, CA, 91343, USA
SO Journal of Neurochemistry (1986), 47(2), 617-24
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
AB Blood plasma hypo- or hyperosmolality alters the concn. of some amino acids in brain tissues of the medial septum and hippocampus of adult Sprague-Dawley rats. With some notable exceptions in this study, brain amino acid concns. decreased under hypoosmotic conditions and increased under hyperosmotic conditions. Osmotic changes and brain amino acid changes appear to be related to each other in an almost linear fashion. A comparison of rats and toads indicated that the patterns of changes in brain amino acid concns. in response to a hypoosmotic plasma osmolality were almost identical for both species. Changes achievable under hyperosmotic conditions were considerably greater in toads. When rats with kindled **epileptogenic** foci were made hypoosmotic by water-loading, seizure thresholds decreased dramatically. The data suggest a possible relationship between the hypoosmotically induced biochem. changes in brain tissues (esp. some amino acid neurotransmitters and neurotransmitter precursors) and the hypoosmotically induced increase in seizure susceptibility.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, blood plasma osmolality effect on, convulsion susceptibility in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

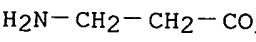
IT **107-95-9 1071-23-4**
RL: BIOL (Biological study)
(of brain, blood plasma osmolality effect on, in rat and toad)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

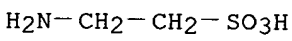
RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-OPO_3H_2$

L23 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1986:418315 CAPLUS
DN 105:18315
TI Effects of GABA-positive drugs on the primary and "mirror" **epileptogenic** foci in the rat hippocampus
AU Gusel, V. A.; Kozlovskii, V. L.
CS Leningr. Pediatr.-Med. Inst., Leningrad, USSR
SO Farmakologiya i Toksikologiya (Moscow) (1986), 49(3), 96-100
CODEN: FATOAO; ISSN: 0014-8318
DT Journal
LA Russian
AB The effects of .beta.-alanine [**107-95-9**], phenybut [1078-21-3], and muscimol [2763-96-4] on the activity of the mirror (MEF) and primary (PEF) **epileptogenic** foci were studied in rats with penicillin-induced epilepsy using direct administration of the drugs into the foci. All 3 compds. decreased the development of seizures both in PEF and MEF. The drugs provoked interseizure epileptiform bursts when administered in the PEF but had no such effect when administered in the MEF. Possible dose-dependent mechanisms of the drugs' actions on GABAergicA and GABAergicB receptors involved in inhibitory control of the activity of **epileptogenic** foci in rat hippocampus were discussed.
IT **107-95-9**
RL: BIOL (Biological study)
(**epileptogenic** foci of hippocampus decrease by)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



L23 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1985:22340 CAPLUS
DN 102:22340
TI GABA and other amino acids in cortical and hippocampal foci removed neurosurgically from epileptic patients
AU Rougier, A.; Loiseau, H.; Cohadon, F.; Lloyd, K. G.; Morselli, P. L.
CS Cent. Hosp. Pellegrin Tripode, Bordeaux, 33076, Fr.
SO Advances in Epileptology (1984), 15th, 43-8
CODEN: ADEPDN; ISSN: 0892-726X
DT Journal
LA English
AB The functional status of GABA synapses together with tissue levels of other putative neurotransmitter amino acids was studied in **epileptogenic** foci (identified by stereo-EEG) removed neurosurgically from several severely epileptic patients unresponsive to antiepileptic medication. L-Glutamic acid decarboxylase was lower than normal in **epileptogenic** cortical tissue from 5 of 6 patients, and was low in **epileptogenic** hippocampal tissue in all 4 patients studied. [3H]GABA A receptor binding was low in all **epileptogenic** tissue examd. GABA levels were unchanged, whereas taurine and glutamate levels were increased in several patients. The ratio of glutamate to GABA levels was higher in **epileptogenic** than in normal tissue in 4 of 7 patients. Apparently, there is a decreased functional activity of GABA synapses in a high proportion of epileptic patients.
IT **107-35-7**
RL: BIOL (Biological study)
(of **epileptogenic** focus of humans)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

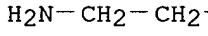


L23 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1984:508440 CAPLUS
DN 101:108440
TI High affinity (3H) .beta.-alanine uptake by scar margins of ferric chloride-induced **epileptogenic** foci in rat isocortex
AU Robitaille, Yvon; Sherwin, Allan
CS Montreal Neurol. Inst., McGill Univ., Montreal, QC, H3A-2B4, Can.
SO Journal of Neuropathology and Experimental Neurology (1984), 43(4), 376-83
CODEN: JNENAD; ISSN: 0022-3069
DT Journal
LA English
AB Cortical astrocytes of normal mammalian brain are endowed with a high affinity uptake system for .beta.-Alanine which is competitively inhibited by gamma aminobutyric acid (GABA), a neurotransmitter strongly implicated in **epileptogenesis**. An evaluation was made of [3H].beta.-Alanine uptake by reactive astrocytes proliferating within scar of **epileptogenic** foci which were induced in rat motor cortex by microinjections of 100 mM ferric chloride. Following in vitro incubation of scar tissue with [3H].beta.-Alanine, ultrastructural morphometry of grain patterns at 5, 30, and 120 days post-injection revealed early and significant grain count increases over astroglial processes, predominantly those related to perivascular glial end-feet. Astrocytic cell body and endothelial cell counts showed a more gradual and stepwise increase. Similar data were obtained by comparing visual and edited mean astrocytic grain counts. These results suggest that the enhanced uptake of reactive astrocytes may reflect a marked decrease of inhibitory GABAergic neurons within ferric chloride-induced scars.
IT **107-95-9**
RL: PROC (Process)
(uptake of, by astrocytes at scar margins of **epileptogenic** foci)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

L23 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1984:172644 CAPLUS
DN 100:172644
TI Taurine- and penicillin-induced epileptic activity
AU Alvarez, A.; Marcano de Cotte, D.; Perez, J. R.; Requena, M. A.; Vallecalle, E.; Drujan, B. D.
CS J.M. Vargas Med. Sch., Univ. Cent. Venezuela, Caracas, Venez.
SO Journal of Neuroscience Research (1984), 11(2), 187-92
CODEN: JNREDK; ISSN: 0360-4012
DT Journal
LA English
AB The effect of i.v. administration of taurine on the elec. activity of the **epileptogenic** focus induced by penicillin applied to the right sensory motor cortex of adult rats was investigated. Taurine (100 mg/kg) was administered 15, 30, 60, and 120 min before the application of penicillin. The EEG was unipolarly recorded by means of electrodes applied to the pia. Taurine caused a decrease of the frequency as well as the spike amplitude of epileptic discharge. The spread of **epileptogenic** foci to the opposite hemisphere was retarded when compared to that of control animals. The maximal antiepileptic effect of taurine was obsd. when the amino acid was administered 30-60 min previous to penicillin. High concns. of taurine in the brain might be necessary to inhibit the epileptic activity.
IT **107-35-7**
RL: BIOL (Biological study)
(epilepsy response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L23 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1982:576457 CAPLUS
DN 97:176457
TI Aspects of the pentylenetetrazol kindling model of **epileptogenesis** in the rat
AU Fabisiak, J. P.; Schwark, W. S.
CS New York State Coll. Vet. Med., Cornell Univ., Ithaca, NY, 14853, USA
SO Experimental Neurology (1982), 78(1), 7-14
CODEN: EXNEAC; ISSN: 0014-4886
DT Journal
LA English
AB The kindling model of **epileptogenesis** is characterized by the induction of a persistent redn. of seizure threshold after repeated exposures of the brain to stimuli which were initially subconvulsive. The ability of repeated injections of pentylenetetrazol (PTZ) [54-95-5] to induce kindling was studied. Subconvulsive doses of PTZ (20-25 mg/kg, i.p.) were administered to rats every 4 days for a total of 21 treatments. The convulsive response score of PTZ-treated rats remained elevated upon challenge with 22.5 mg/kg PTZ after a 3-wk PTZ-free period. Studies on the mechanisms involved in PTZ-induced kindling revealed that hepatic microsomal cytochrome P 450 [9035-51-2] concns. were unchanged after chronic PTZ treatment. No significant changes in brain amino acids, including GABA [56-12-2] and taurine [**107-35-7**], 2 neuroinhibitory amino acids which have been implicated in the regulation of seizure phenomena, were found in PTZ-kindled animals.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, pentylenetetrazol kindling in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



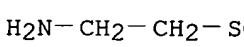
L23 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1981:597643 CAPLUS
DN 95:197643
TI Thalamic generalized seizure induced by tungstic acid gel in cats and its suppression by anticonvulsants
AU Hori, Misako; Ito, Tsugutaka; Shimizu, Masanao
CS Res. Lab., Dainippon Pharm. Co., Ltd., Osaka, 564, Japan
SO Japanese Journal of Pharmacology (1981), 31(5), 771-9
CODEN: JJPAAZ; ISSN: 0021-5198
DT Journal
LA English
AB The expts. were performed electroencephalog. on gallamine-immobilized cats with the thalamic foci induced by application of tungstic acid [11105-11-6] gel (gel). The gel (50 .mu.L) applied to nucleus centralis lateralis (CL) caused generalized seizure (GS) with high frequency components triggered by slow wave, and GS recurred with a regular interictal period. The application to nucleus centralis medialis or nucleus medialis dorsalis did not induce recurring GS, indicating the heterogeneity in the **epileptogenesis** of the thalamus. The GS induced by the gel application to the CL was of thalamic origin. Anticonvulsants used were found to prolong the interictal period of the GS, without modifying its duration. There was a difference between the drugs effective against grand mal and petit mal epilepsies in that the prolongation by the former drugs, diphenylhydantoin Na [630-93-3] and phenobarbital Na [57-30-7] was more pronounced at low doses than that by the latter drugs, trimethadione [127-48-0] and dipropylacetate Na [1069-66-5]. Apparently, the gel-induced epileptic model with thalamic foci is useful for analyzing the pathophysiol. process of epilepsy and for evaluating the drugs effective against grand mal epilepsy.
IT **107-35-7**
RL: BIOL (Biological study)
(seizure from brain thalamus application of tungstic acid gel response to, grand-mal epilepsy response in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L23 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1981:478148 CAPLUS
DN 95:78148
TI Amino acid abnormalities in **epileptogenic** foci
AU Perry, Thomas L.; Hansen, Shirley
CS Dep. Pharmacol., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.
SO Neurology (1981), 31(7), 872-6
CODEN: NEURAI; ISSN: 0028-3878
DT Journal
LA English
AB The amino acid contents of 54 **epileptogenic** foci removed neurosurgically from temporal or frontal cortex of 35 patients with focal epilepsy were compared with those of biopsies from the same cortical regions of 14 nonepileptic patients. Neither the taurine nor GABA content was reduced in **epileptogenic** foci. The glycine content was elevated in some foci, whereas the aspartic acid content was normal. The glutamic acid content was higher in **epileptogenic** foci than in control cortex, and foci contained amts. of glutamate more than 2 std. deviation units above the control mean. The findings do not support hypotheses that deficiencies of taurine or GABA are involved in the pathogenesis of focal epilepsy, but suggest a possible etiol. role for the excitatory neurotransmitter, glutamic acid.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, in focal epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L23 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1980:400815 CAPLUS
DN 93:815
TI Role of calcium ions in the development of the anticonvulsant effect of taurine
AU Gurevich, V. S.; Tkachenko, E. I.; Kulikova, O. G.
CS Inst. Exp. Med., Leningrad, USSR
SO Byulleten Eksperimental'noi Biologii i Meditsiny (1980), 89(4), 418-20
CODEN: BEBMAE; ISSN: 0365-9615
DT Journal
LA Russian
AB In seizure-prone rats, brain cortex microsomes had less Ca2+,Mg2+-dependent ATPase [9000-83-3] and decreased Ca2+ binding in comparison with normal rats; taurine [**107-35-7**] increased ATPase activity in and Ca2+ binding by brain microsomes from both normal and seizure-prone rats. Taurine prevented seizures in rabbits with penicillin-provoked **epileptogenic** focus. However, when EGTA was injected together with taurine the anticonvulsant effect was no longer obsd., suggesting the importance of Ca2+ in this effect.
IT **107-35-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, calcium in)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1980:140633 CAPLUS
DN 92:140633
TI Effect of anticonvulsants on spiking activity induced by cortical freezing in cats
AU Hori, M.; Ito, T.; Yoshida, K.; Shimizu, M.
CS Res. Lab., Dainippon Pharm. Co., Ltd., Suita, 564, Japan
SO Epilepsia (1979), 20(1), 25-36
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB In an attempt to know whether the existing anticonvulsants act on **epileptogenic** focus, the effect on spiking activity (SA) induced by freezing of the visual cortex was examd. in gallamine-immobilized cats. The SA was localized in the neighbor or ipsilateral cortex of the freezing area; little epileptiform activity was produced in the contralateral anterior cortex, and ipsilateral thalamus and hippocampus. Spike frequency and its amplitude were stable over 8 h. Diazepam [439-14-5] suppressed SA and decreased spike frequency and its amplitude. Na dipropylacetate [1069-66-5] and acetazolamide Na [1424-27-7] also suppressed SA. On the other hand, phenobarbital Na [57-30-7], carbamazepine [298-46-4], and a high dose of phenytoin Na [630-93-3] enhanced SA and increased the spike frequency. Low doses of phenytoin and trimethadione [127-48-0] were without effect in this aspect. Taurine [**107-35-7**] suppressed SA and changed the spikes to wave-like forms. The EEG arousal response was depressed with phenobarbital, carbamazepine, diazepam, and high dose of phenytoin, but not with the other drugs examd. From these results, it is suggested that diazepam, dipropylacetate, acetazolamide, and taurine depress the **epileptogenic** focus activity itself without relation to the activating system.
IT **107-35-7**
RL: BIOL (Biological study)
(**epileptogenic** spiking activity response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

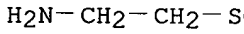
L23 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1980:476 CAPLUS
DN 92:476
TI Action of inhibitory amino acids on acute epileptic foci: an electrographic study
AU Fariello, Ruggero G.
CS Clin. Sci. Cent., Univ. Wisconsin, Madison, WI, 53792, USA
SO Experimental Neurology (1979), 66(1), 55-63
CODEN: EXNEAC; ISSN: 0014-4886
DT Journal
LA English
AB Epileptiform activity was induced in adult cats anesthetized with Ketamine or Na pentobarbital. Acute models of focal epilepsy were created by application of various **epileptogenic** agents to neocortical or limbic structures. Inhibitory amino acids were injected i.v. and their effects on epileptiform discharges monitored for 2 h after administration. Amino acid solns. were adjusted to pH between 5.5 and 8. Glycine [56-40-6] (to 250 mg/kg) did not induced any change. Short-lasting inhibitory effects (5 s to 9 min) were noted with .beta.-alanine [**107-95-9**], .gamma.-aminobutyric acid (GABA) [56-12-2] (>80 mg/kg), taurine [**107-35-7**] (>50 mg/kg), and 3-aminopropanesulfonic acid [3687-18-1] (3-APS, >5 mg/kg). The action of 3-APS was particularly powerful in abolishing cortical spiking with only moderate depression of background EEG activity. GABA, taurine, and 3-APS also induced depression of respiration in animals under barbiturate anesthesia. In addn., 3-APS caused a 20% decrease in systolic blood pressure. Similar and even greater pressure decreases were obsd. after injection of control drugs which did not, however, affect the epileptic firing rate. 3-APS seems to deserve further investigation as a possible antiepileptic and GABA-mimetic agent.
IT **107-35-7 107-95-9**
RL: BIOL (Biological study)
(antiepileptic activity in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

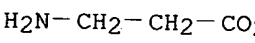
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

L23 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1979:432866 CAPLUS
DN 91:32866
TI Augmentation of thalamo-motor cortico-cerebellar **epileptogenesis** by taurine and its antagonism by diphenylhydantoin
AU Frigyesi, Tamas L.; Lombardini, J. B.
CS Sch. Med., Texas Tech Univ., Lubbock, TX, 79430, USA
SO Life Sciences (1979), 24(14), 1251-9
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB An acute penicillin focus was established in the motor cortex of cats. Surface recordings were obtained from the penicillin focus; focal potentials were recorded from the ipsilateral thalamic ventrolateral nucleus and the contralateral cerebellar Purkinje layer. The interictal spike relations were 1:1:1 at these recording sites. The effects of systemically administered taurine [**107-35-7**] were compared with those of diphenylhydantoin (I) [630-93-3] which was administered either systemically or topically onto the penicillin focus. Two epileptic attributes were explored: thalmo-corticocerebellar ictal episodes (their incidence, durations and tonic-clonic manifestations), and interictal excitatory potentials in the Punkinje layer. Taurine and I exhibited disparate effects on these parameters of epilepsy: the incidence and durations of ictal, and the proportions of tonic-clonic bursts were increased by taurine and decreased by I; and the interictal excitatory potentials in the Purkinje layer were enhanced by taurine and reduced by I. Inasmuch as I effects are potent antiepileptic, taurine appears to be, at least a short-term, potent **epileptogen** in this exptl. model of epilepsy.
IT **107-35-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epileptogenic** activity of)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1979:166111 CAPLUS
DN 90:166111
TI An experimental model to investigate disinhibitory mechanisms in penicillin **epileptogenesis**
AU Marsan, C. Ajmone
CS NIH, Bethesda, MD, USA
SO Electroencephalography and Clinical Neurophysiology, Supplement (1978), Volume Date 1977, 34(Contemp. Clin. Neurophysiol.), 285-7
CODEN: EECSB3; ISSN: 0424-8155
DT Journal
LA English
AB L-Homocysteic acid (HC) and penicillin both caused increased elec. discharge when applied to the cerebral somatosensory cortex of the cat. .gamma.-Aminobutyric acid (GABA), glycine, and .beta.-alanine each inhibited the elec. discharges produced by HC. However, the penicillin-induced elec. activity was more resistant to the effects of GABA than was the HC-induced activity. Only a weak and non-specific antagonism was obsd. between penicillin and the above amino acids after HC administration. Thus, the **epileptogenic** action of penicillin cannot be attributed exclusively to interference with the action of inhibitory amino acids. An obsd. simply additive effect of penicillin and HC also indicates that the **epileptogenic** action of penicillin is not due to induction of postsynaptic hypersensitivity to excitatory neurotransmitters.
IT **107-95-9**
RL: BIOL (Biological study)
(in penicillin-induced epilepsy)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



L23 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1978:457916 CAPLUS
DN 89:57916
TI Lack of correlation between taurine levels in 16 brain regions and paroxysmal discharges in the thalamocortical circuit
AU Frigyesi, Tamas L.; Lombardini, J. B.
CS Dep. Physiol., Texas Tech Univ. Sch. Med., Lubbock, TX, USA
SO Neuroscience Letters (1978), 7(2-3), 213-17
CODEN: NELED5; ISSN: 0304-3940
DT Journal
LA English
AB Status epilepticus was induced in cats with a penicillin focus in their motor cortex. Taurine content was detd. in the penicillin focus and in 15 other brain regions. Under this condition taurine levels were predominantly decreased in some cats and remained unchanged or significantly increased in others. In the exptl. group, the av. concn. of taurine was not significantly different from that of the control group. Thus, the data fail to support the hypothesis that decreased levels of taurine in the epileptic focus or in supraspinal structures are causally related to penicillin **epileptogenesis**.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain in epilepsy exptl. induced)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

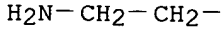
L23 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1977:165426 CAPLUS
DN 86:165426
TI Relations between electroencephalographic pattern and biochemical picture of the cobalt **epileptogenic** lesion after cortical superfusion with taurine
AU Durelli, Luca; Mutani, Roberto; Quattrocolo, Giovanni; Delsedime, Michele; Buffa, Carlo; Fassio, Franco; Valentini, Consuelo; Fumero, Sandro
CS Med. Sch., Univ. Turin, Turin, Italy
SO Experimental Neurology (1977), 54(3), 489-503
CODEN: EXNEAC; ISSN: 0014-4886
DT Journal
LA English
AB Co gelatin pellets were implanted into the feline cortex pretreated with a superfusion of taurine [**107-35-7**]. Taurine superfusion remarkably delayed the onset and subsequent development of focal epileptic activity. At the end of superfusion, the taurine cortical concn. was highly increased whereas the glutamic acid [56-86-0] level was reduced. The appearance and evolution of focal epileptic discharges was paralleled by a progressively more extensive decrease in concn. of several amino acids. A relation between the taurine and glutamate levels and the depression of epileptic susceptibility of cortex was pointed out. Alterations of cortical amino acid content in the Co focus were more severe in comparison with the penicillin focus under the same exptl. conditions. The taurine-induced prolonged suppression of focal epileptic activity was assocd. with epileptiform electroencephalog. abnormalities recorded in cortical regions far from the site of cobalt implantation. These extrafocal spikes occurred before the onset of the focal activity and decreased, even disappeared, simultaneously with progressive enhancement of the epileptic discharges in the cobalt area. Thus, Co, though topically implanted, might exert an **epileptogenic** action diffuse to different regions of the brain. Under normal conditions the inhibition by the **epileptogenic** focus in the Co area would not allow the simultaneous development of other **epileptogenic** zones. The latter would, however, develop if the first zone had been previously inhibited by the local action of taurine.
IT **107-35-7**
RL: BIOL (Biological study)
(cobalt-induced epilepsy response to, amino acids of brain in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

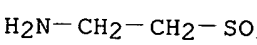
L23 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1977:153550 CAPLUS
DN 86:153550
TI Longitudinal changes of brain amino acid content occurring before, during and after epileptic activity
AU Mutani, R.; Durelli, L.; Mazzarino, M.; Valentini, C.; Monaco, F.; Fumero, S.; Mondino, A.
CS Med. Sch., Turin Univ., Turin, Italy
SO Brain Research (1977), 122(3), 513-21
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB In cats affected with cortical **epileptogenic** foci induced by penicillin application to and Co implantation into the pericruciate area, the brain amino acids contents were detd. in the focus as well as in extrafocal areas. In different groups of animals, brain removal for biochem. detns. was performed at different times before, during, and after epilepsy and the values compared to controls. The only amino acid to show a significant change before appearance of spikes in both types of epilepsy was taurine, which decreased. Co epilepsy was accompanied by changes in a larger no. of amino acids than penicillin epilepsy: in the former the brain content of taurine, GABA, aspartate, glutamate, serine, threonine, glycine, and alanine was altered. The changes were proportional to the severity of epilepsy and more prominent in the focus area. After disappearance of spikes the levels of most amino acids returned to normal except for some amino acids, previously unaffected by penicillin epilepsy, which were decreased. Thus, the decrease in brain taurine, occurring before the appearance of penicillin and Co epilepsy, could increase the excitability of a certain neuronal population and thus, by potentiating the effects on neurons of penicillin and Co, contribute to the initiation of epilepsy.
IT **107-35-7**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(of brain, in epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L23 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1976:472414 CAPLUS
DN 85:72414
TI Electroencephalographic and biochemical study of the antiepileptic action of taurine administered by cortical superfusion
AU Durelli, L.; Mutani, R.; Delsedime, M.; Quattrocolo, G.; Buffa, C.; Mazzarino, M.; Fumero, S.
CS Med. Sch., Univ. Turin, Turin, Italy
SO Experimental Neurology (1976), 52(1), 30-9
CODEN: EXNEAC; ISSN: 0014-4886
DT Journal
LA English
AB After cortical superfusion with taurine [**107-35-7**], an electroencephalographc and biochem. study was performed in cats affected with unilateral and bilateral penicillin **epileptogenic** foci. Taurine-treated cats showed a depressed epileptic susceptibility of the cortex, which was more remarkable in the less severe epileptic picture produced by unilateral penicillin. Both in control and in **epileptogenic** cortex, at the end of taurine superfusion, the amino acid content in brain was altered only for taurine and glutamic acid [56-86-0], which were increased and decreased, resp. The subsequent changes in the brain concn. of these 2 compds. were the opposite, i.e., taurine decreased and glutamate increased, and a significant neg. correlation between the cortical concns. of the 2 amino acids was calcd. The rapidity of the changes was greater in **epileptogenic** than in control cortex, and max. in the severe epilepsy produced by bilateral penicillin. Furthermore, the rapidity of the changes decreased during and after the disappearance of spikes. The hypothesis is put forward that the changes in brain content of taurine and glutamate obsd. after taurine cortical loading share the responsibility for the depressed epileptic susceptibility of the cortex. The common enzyme involved in the metab. of taurine and glutamate could be responsible for the neg. correlation between the 2 compds.
IT **107-35-7**
RL: BIOL (Biological study)
(antiepileptic activity of, brain taurine and glutamate in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

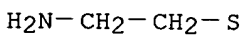


L23 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1976:103509 CAPLUS
DN 84:103509
TI Taurine content of **epileptogenic** foci in human brain
AU Perry, Thomas L.; Hansen, Shirley
CS Dep. Pharmacol., Univ. British Columbia, Vancouver, BC, Can.
SO Taurine, [Int. Symp.], 1st (1976), Meeting Date 1975, 275-81. Editor(s): Huxtable, Ryan; Barbeau, Andre. Publisher: Raven, New York, N. Y. CODEN: 32IHAG
DT Conference
LA English
AB **Epileptogenic** foci were obtained from epilepsy patients who underwent removal of cortical tissue. As controls, cortical biopsies were obtained from nonepileptogenic patients. Taurine and .gamma.-aminobutyric acid levels of the foci generally were in or above the upper range of normal. Glycine level of the foci was in the high normal or was markedly elevated. Aspartic and glutamic acids were not decreased in the foci but glutathione was increased. The taurine content in the **epileptogenic** foci of frontal and temporal cortex was highly significantly elevated when compared with the taurine content on nonepileptic frontal and temporal cortex.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain **epileptogenic** foci)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

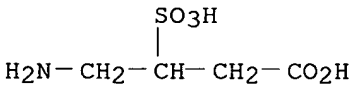


L23 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1972:560171 CAPLUS
DN 77:160171
TI Amino acids in the cobalt-induced **epileptogenic** and nonepileptogenic cat's cortex
AU Koyama, Ikuko
CS Dep. Physiol., Univ. Montreal, Montreal, QC, Can.
SO Canadian Journal of Physiology and Pharmacology (1972), 50(8), 740-52
CODEN: CJPPA3; ISSN: 0008-4212
DT Journal
LA English
AB **Epileptogenic** cortical foci were produced by topical application of cobalt [7440-48-4] powder to the exposed anterior or posterior sigmoid gyrus of adult cats, and within 60-90 min, epileptic discharges were obsd. only in the area adjacent to the Co-treated focus. Tonic and clonic epileptic convulsions occurred 24 hr later, but the seizures disappeared by the 3rd day after treatment. Concns. of glutamic acid [56-86-0], aspartic acid [56-84-8], and .alpha.-aminobutyric acid [80-60-4] were decreased in the cortical tissue adjacent to the Co application site, and glycine [56-40-6], threonine [72-19-5], serine [56-45-1], and taurine [**107-35-7**] concns. increased markedly during the convulsive period. The rate of glutamic acid release increased within 90 min after Co application along with a corresponding decrease of the rate of release of glutamine [56-85-9] and urea [57-13-6]. The excitatory effect of the liberated glutamic acid may be important in the production of focal epileptic discharges following the application of Co powder to the cerebral cortex.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, cobalt-induced convulsion in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

L23 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1972:473481 CAPLUS
DN 77:73481
TI Amino acid content of **epileptogenic** human brain. Focal versus surrounding regions
AU Van Gelder, N. M.; Sherwin, A. L.; Rasmussen, T.
CS Cent. Res. Neurol. Sci., Univ. Montreal, Montreal, QC, Can.
SO Brain Research (1972), 40(2), 385-93
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Amino acid anal. of tissues from **epileptogenic** foci and surrounding tissues in human brain showed lower than normal levels of .gamma.-aminobutyric acid and aspartic acid in all regions. Lower glutamic acid and taurine and very high glycine levels characterized the most hyperexcitable areas. Amino acid comparisons on the same patient demonstrated that the focal area contained the lowest concns. of glutamic acid, aspartic acid, and taurine in combination with the highest glycine content. The results indicate that in **epileptogenic** cortex an uncoupling has occurred between glucose oxidn. and amino acid metabolism. Protein metabolism may be impaired in addn. or as a consequence of the uncoupling.
IT **107-35-7**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(of brain, in epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L23 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2003 ACS
AN 1970:519019 CAPLUS
DN 73:119019
TI Electrophysiological and clinical studies on inhibitory actions of .gamma.-amino butyric acid and its derivatives. I. Electrophysiological study
AU Sugatani, Hiroshi
CS Med. Sch., Okayama Univ., Okayama, Japan
SO Okayama Igakkai Zasshi (1969), 81(9-10), 505-18
CODEN: OIZAAV; ISSN: 0030-1558
DT Journal
LA Japanese
AB The inhibitory action of .gamma.-amino-.beta.-hydroxybutyric acid (I), .gamma.-amino-.beta.-sulfonylbutyric acid (II), and .gamma.-amino-.beta.-phenylbutyric acid (III) on the central nervous system was investigated in dogs, cats, and human subjects. The application of I and II solns. on the **epileptogenic** cortical focus of human epileptics was performed and the corticogram was recorded with ref. to spikes and after-discharges to examine the anticonvulsive actions of these solns. Application of II on the cerebral cortex of dogs showed low-voltage activity and spiking activity in the corticogram. III caused spiking activity, developing to the generalized convulsive seizure pattern. The spiking activity caused by II and III was inhibited by I. II did not inhibit the after-discharge or spiking activity on the **epileptogenic** cortical focus of human epileptics. However, I showed a strong inhibitory action to after-discharge and spiking activity. Application of I on the cerebral cortex reversed the cortical evoked potentials caused by elec. stimulation of the thalamus in cats. It was suggested that I has an inhibitory action on the cerebral cortex, but II and III do not.
IT **22515-54-4**
RL: BIOL (Biological study)
(brain response to, in epilepsy)
RN 22515-54-4 CAPLUS
CN Butanoic acid, 4-amino-3-sulfo- (9CI) (CA INDEX NAME)



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L24        3622 CONVULSIV?

=> s l18 and l24
L25          41 L18 AND L24

=> s l25 not l23
L26          36 L25 NOT L23

=> d l26 1-36 bib,ab,hitstr
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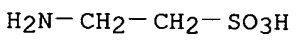
L26 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 2001:387705 CAPLUS
DN 136:81061
TI **Convulsive** effects and mechanism of tetramethylenedisulfotetramine
AU Zhang, Chunying; Zhu, Tongjun; Chen, Xingyan; Hu, Guoxin; Liu, Dingxin
CS Wenzhou Medical College, Department of Pharmacology, 325027, Peop. Rep. China
SO Weisheng Dulixue Zazhi (2001), 15(1), 5-7
CODEN: WDZAEK; ISSN: 1002-3127
PB Beijingshi Laodong Weisheng Zhiyebing Fangzhi Yanjiuso
DT Journal
LA Chinese
AB The **convulsive** effects and mechanism of tetramethylenedisulfotetramine were studied. Ninety-seven percent of **convulsive** dose (CD97) was detd., the levels free amino acid was measured by using amino acid automated analyzer in mice brain, [3H]-.gamma.-aminobutyric acid (GABA) binding sites in mice brain were obsd. by autoradiog., and d. was detd. by image anal. system. CD97 was 0.384 mg kg-1 [(0.337-0.431) mg kg-1] in acutely poisoned mice. The content of free GABA was significantly increased, glutamic acid was decreased, and the changes of the other amino acids were no significant in mice brain. The lowered d. of different brain regions was obsd. The results showed that TET had strong stimulating effect on the central nervous system, and animal death may be related to respiratory failure caused by continuous seizure of tetanic convulsion in acutely poisoned animals, and **convulsive** mechanisms may be related to direct inhibition of [3H]-GABA binding with its receptor.
IT **107-35-7**, Taurine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**convulsive** effects and mechanism of tetramethylenedisulfotetramine)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 2 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 2000:875349 CAPLUS
DN 135:75140
TI Action of 4-aminopyridine on extracellular amino acids in hippocampus and entorhinal cortex: a dual microdialysis and electroencephalographic study in awake rats
AU Medina-Ceja, L.; Morales-Villagran, A.; Tapia, R.
CS Departamento de Biologia Celular y Molecular, CUCBA, Universidad de Guadalajara, Guadalajara, Jal., Mex.
SO Brain Research Bulletin (2000), 53(3), 255-262
CODEN: BRBUDU; ISSN: 0361-9230
PB Elsevier Science Inc.
DT Journal
LA English
AB To study the role of amino acids in the hippocampus and the entorhinal cortex during the **convulsive** process induced by 4-aminopyridine (4-AP), we have used a device allowing the simultaneous microdialysis and the recording of their elec. activity of both regions in freely moving rats. We found that infusion of 4-AP into the entorhinal cortex resulted in a large increase in extracellular glutamate and glutamine and small increases in glycine and taurine levels. Likewise, infusion of 4-AP into the hippocampus resulted in a major increase in glutamate, as well as slight increases in taurine and glycine. In both infused regions the peak concn. of extracellular glutamate was obsd. 15 min after 4-AP administration. No significant changes were found in the non-infused hippocampus or entorhinal cortex of the same rats. Simultaneous electroencephalog. recordings showed intense epileptiform activity starting during 4-AP infusion and lasting for the rest of the expt. (1 h) in both the entorhinal cortex and the hippocampus. The discharges were characterized by poly-spikes and spike-wave complexes that propagated almost immediately to the other region studied. These findings suggest that increased glutamatergic synaptic function in the circuit that connects both regions is involved in the epileptic seizures induced by 4-AP.
IT **107-35-7**, Taurine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(action of 4-aminopyridine on extracellular amino acids in hippocampus and entorhinal cortex: a dual microdialysis and electroencephalog. study in awake rats)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 2000:417441 CAPLUS
DN 133:333339
TI Relation between the content of mediator amino acids in brain structures and the level of **convulsive** readiness in rats
AU Yakimenko, T. I.
CS Khar'kov. Gos. Med. Univ., MZ Ukrainy, Kharkov, Ukraine
SO Neirofiziologiya (1999), 31(6), 486-491
CODEN: NEFZB2; ISSN: 0028-2561
PB Institut Fiziologii im. A. A. Bogomol'tsa NAN Ukrainy
DT Journal
LA Russian
AB Changes in the synaptosomal levels of glutamate (Glu), taurine (Tau), glycine, and glutamine (Gln), were studied after multiple acoustic stimulations. Changes were more frequent, or larger, after polystimulation. In seizure-prone sublines, after a single or repeated seizures, an increase in synaptosomal glutamate was obsd. These data support the hypothesis that alterations in the balance between excitatory and inhibitory amino acids may be involved in the expression of epilepsy.
IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(correlation between the content of mediator amino acids in brain structures and level of **convulsive** readiness in rats)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 2000:155825 CAPLUS
DN 133:15882
TI The effect of pentylenetetrazole-kindling on the extracellular glutamate and taurine levels in the frontal cortex of rats
AU Li, Z.-q.; Yamamoto, Y.; Morimoto, T.; Ono, J.; Okada, S.; Yamatodani, A.
CS Faculty of Medicine, School of Allied Health Science, Department of Medical Physics, Osaka University, Suita, Osaka, Japan
SO Neuroscience Letters (2000), 282(1,2), 117-119
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The extracellular concns. of glutamate and taurine were studied in the frontal cortex of freely-moving pentylenetetrazole (PTZ)-kindled rats using an in vivo microdialysis. A significant and sustained increase in the glutamate level was obsd. in the kindled rats, in contrast, a slight and delayed increase was obsd. in the non-kindled rats when the same grade seizure was induced by PTZ. The **convulsive** dose of PTZ administration caused a decrease in taurine levels in the controls, however, no significant changes were found in the kindled rats.
IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(effect of pentylenetetrazole-kindling on extracellular glutamate and taurine levels in frontal cortex of rats)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 2000:34961 CAPLUS
DN 132:73661
TI Cells and animals deficient in the .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics
IN Messing, Robert O.; Hodge, Clyde W.
PA USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000001805	A1	20000113	WO 1999-US15152	19990702
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	US 2002151465	A1	20021017	US 2002-39278	20020104
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	WO 1999-US15152	W	19990702		
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AB Cells and animals deficient in protein kinase C .epsilon. isoenzyme (PKC.epsilon.) that can be used to screen for anti-anxiety drugs are described. According to the present invention, PKC.epsilon.-inhibiting compds. act in synergy with drugs acting at the GABAA receptor. These modulators of PKC.epsilon. may also be used to modulate alc. consumption, self-administration of other drugs of abuse, and the effects of alc. consumption. PKC.epsilon. inhibitors may also also be used either alone or in conjunction with allosteric agonists of GABAA receptors, to treat conditions, such as addiction, withdrawal syndrome, skeletal muscle spasms, **convulsive** seizures, and epilepsy, that are amenable to treatment by allosteric agonists of GABAA receptors. Addnl. aspects of the present invention are diagnostic methods for identifying individuals at risk for becoming alcoholics or abusers of other drugs and kits for performing such diagnostic methods. Transgenic homozygous PKC.epsilon. knockout mice were found to show lower levels of anxiety than control animals. Gross anatomy of the knockout mice is essentially normal, but there are changes in the patterns of fiber outgrowth and branching in the

stratum radiatum. The knockout mice showed lower levels of alc. consumption in ethanol preference drinking tests with a 75% lowering of ethanol preference but did no show any altered preference for sweet (saccharin) or bitter (quinine) flavors or change in general caloric intake. These mice were also hypersensitive to the sedating effects of alc. and to the allosteric GABAA agonists pentobarbital and diazepam.

IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(altered levels of, in PKC.epsilon. knockout mice; cells and animals deficient in .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics)

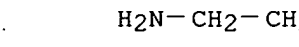
RN 107-35-7 CAPLUS

CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

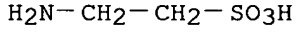
$H_2N-CH_2-CH_2-SO_3H$

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1997:663972 CAPLUS
DN 128:10944
TI Release of dopamine, GABA and EAA in rats during intrastriatal perfusion with kainic acid, NMDA and soman: a comparative microdialysis study
AU Jacobsson, Stig O. P.; Cassel, Gudrun E.; Karlsson, Britt M.; Sellstrom, Ake; Persson, Sven-Ake
CS Department of Biomedicine, Defence Research Establishment (FOA), Division of NBC Defence, Umea, S-901 82, Swed.
SO Archives of Toxicology (1997), 71(12), 756-765
CODEN: ARTODN; ISSN: 0340-5761
PB Springer
DT Journal
LA English
AB There is an increasing amt. of exptl. evidence that excitatory amino acids (EAAs) are involved in the brain lesions obsd. after severe intoxication with the highly toxic organophosphorus compd. soman. This study was undertaken to compare the acute actions of soman, and the glutamatergic receptor agonists kainic acid and N-methyl-d-aspartate (NMDA) on striatal release of dopamine and amino acids. The neurotoxic compds. were administered in high (10 mM) concns. by unilateral intrastriatal microdialysis perfusion in freely moving rats. During the microdialysis the animals were obsd. for toxic signs related to convulsion. The glial fibrillary acidic protein (GFAP) was monitored as a marker of neurotoxicity in parts of prefrontal cortex, hippocampus, striatum and cerebellum. Acetylcholinesterase (AChE) inhibition in six brain regions was measured after soman perfusion in order to assess its cerebral distribution. The authors found that soman perfusion induced a major release of dopamine, GABA and aspartate in the striatum. Kainic acid also induced a release of dopamine and aspartate. NMDA was not as potent an inducer of striatal neurotransmitter release as soman and kainic acid. Soman and kainic acid perfusion produced **convulsive** behavior in the rats. The main neurochem. event in the striatum during soman- and kainate-induced convulsions is the release of dopamine. The authors suggest that this major dopamine release might be as important as an increase in EAA in the cascade of pathol. events leading to the brain damage in the striatum obsd. after soman intoxication.
IT **107-35-7**, Taurine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(release of dopamine, GABA and EAA in rats during intrastriatal perfusion with kainic acid, NMDA and soman - a comparative microdialysis study)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



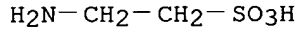
L26 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1997:452539 CAPLUS
DN 127:174855
TI Co-variation of free amino acids in brain interstitial fluid during pentylenetetrazole-induced **convulsive** status epilepticus
AU Sechi, GianPietro; Rosati, Giulio; Deiana, Giovanni A.; Petruzzi, Valentino; Deriu, Franca; Correddu, Paola; De Riu, Pier Luigi
CS Neurological Clinic, University of Sassari, Viale S. Pietro 10, Sassari, 07100, Italy
SO Brain Research (1997), 764(1,2), 230-236
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier
DT Journal
LA English
AB Effects of pentylenetetrazole (PTZ)-induced **convulsive** status epilepticus on free amino acids changes in venous blood, CSF and interstitial fluid (IF) of the brain were examd. in dogs. A vol. of brain IF sufficient for anal. was obtained by chronically implanted tissue cages. The onset of PTZ-induced **convulsive** seizures seemed mainly related to a marked increase of glutamate, aspartate, taurine, glycine and phosphoserine while, the maintenance and frequency of seizures seemed related to a marked increase of serine and glycine, in combination with a moderate rise of glutamate. L-.alpha.-Aminoadipate was recovered in moderate amt. in epileptic brain IF, while, in controls, this compd. was present in minimal amt. The obsd. complex temporal variation of the amino acidic pattern may play a role in PTZ-induced seizures and, possibly, in pharmacol. kindling and brain structural alterations induced by PTZ.
IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(co-variation of free amino acids in brain interstitial fluid during pentylenetetrazole-induced **convulsive** status epilepticus in relation to cerebrospinal fluid)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1995:326694 CAPLUS
DN 122:96356
TI Effects of 3,4-dichlorophenylpropenoyl-sec-butylamine on **convulsive** seizures induced by kainic acid
AU Liu, Fujun; Tao, Cheng
CS Dep. Pharmacol., Beijing Med. Univ., Beijing, 100083, Peop. Rep. China
SO Zhongguo Yaolixue Yu Dulixue Zazhi (1994), 8(4), 305-6
CODEN: ZYYZEW; ISSN: 1000-3002
PB Zhongguo Yaolixue Yu Dulixue Zazhi Biarjibu
DT Journal
LA Chinese
AB The antiepileptic effects and mechanisms of the title amine (DCPB) were investigated in seizures induced by kainic acid (KA). DCPB antagonized the epileptic seizures induced by intracerebroventricular administration of KA in mice, by s.c. injection of KA in rats and by hippocampal injection of KA in rabbits. DCPB elevated brain levels of GABA and reduced those of glutamic acid and aspartic acid, but it did not affect those of glycine and taurine. These effects may be related to its antiepileptic action.
IT **107-35-7**, Taurine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(amino acids of brain response to antiepileptic action of dichlorophenylpropenoyl-sec-butylamine)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

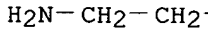
L26 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1992:424160 CAPLUS
DN 117:24160
TI Drug-induced seizures in taurine-deficient mice
AU Shimada, Chiaki; Tanaka, Shuichi; Sano, Mitsuo; Araki, Hiromasa
CS Res. Dev. Cent., Fuso Pharm. Ind., Ltd., Osaka, 536, Japan
SO Yakubutsu, Seishin, Kodo (1991), 11(4), 257-60
CODEN: YSKODB; ISSN: 0285-5313
DT Journal
LA Japanese
AB Pentetrazole-, picrotoxin- and strychnine-induced seizures in taurine-deficient mice produced by treatment with guanidinoethyl sulfonate (GES), a taurine transport antagonist, were investigated. Mice were fed a taurine-free diet and water contg. 1% GES from 2 wk of pregnancy to weaning. The same feeding condition was applied to male offspring from 3 wk of age. At 5 wk of age, convulsants were administered to some mice and the others were sacrificed for detn. of brain amino acid concns. The incidences of both seizure and death for strychnine and death for picrotoxin were enhanced by treatment with GES, whereas the latency of pentetrazole-induced tonic extensor was prolonged. Significant decrease of brain taurine, asparagine and GABA concns. were obsd. in mice treated with GES. These results suggest that **convulsive** seizures caused by disinhibition of taurine and GABA system are enhanced by deficiency of brain taurine level.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(deficiency of, seizures induced by GABA or taurine disinhibition enhancement by, amino acids of brain in)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1990:550024 CAPLUS
DN 113:150024
TI Regional excitatory and inhibitory amino acid levels in epileptic El mouse brain
AU Hiramatsu, Midori; Edamatsu, Rei; Suzuki, Shigeo; Shimada, Masakazu; Mori, Akitane
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Neurochemical Research (1990), 15(8), 821-5
CODEN: NEREDZ; ISSN: 0364-3190
DT Journal
LA English
AB Inbred mutant El mice are highly susceptible to **convulsive** seizures upon tossing stimulation. The levels of excitatory (glutamate and aspartate), inhibitory (GABA) were examd. in discrete brain regions of stimulated El mice [El(+)], non-stimulated El mice [El(-)], and ddY mice which do not have the **convulsive** disposition. In comparison with ddY, increased levels of aspartate, glutamate, glutamine, and taurine were detected in brain regions of El(-). The levels of GABA and glycine were almost the same in ddY and El(-). Compared to El(+), the levels of aspartate, glutamate, glutamine, and GABA in El(-) were the same or higher. In the case of taurine and glycine, the levels in El(-) were the same or lower than those in El(+). Alanine in El(-) had higher levels than those in El(+) in the hippocampus but lower in the cerebellum. While marked changes were registered in several brain regions, none of the amino acids investigated showed any differences in the hypothalamus of the various groups of mice.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain regions, epilepsy susceptibility in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1989:625241 CAPLUS
DN 111:225241
TI Chronic lithium treatment and status epilepticus induced by lithium and pilocarpine cause selective changes of amino acid concentrations in rat brain regions
AU Jope, Richard S.; Miller, Joanne M.; Ferraro, Thomas N.; Hare, Theodore A.
CS Dep. Pharmacol., Univ. Alabama, Birmingham, AL, 35294, USA
SO Neurochemical Research (1989), 14(9), 829-34
CODEN: NEREDZ; ISSN: 0364-3190
DT Journal
LA English
AB The effects of 4 wk of dietary Li+ treatment and of status epilepticus induced by administration of pilocarpine to Li+-treated rats were examd. on the concns. of amino acids in 4 regions of rat brain: cerebral cortex, hippocampus, striatum, and substantia nigra. To ensure accurate quantitation of the amino acids, animals were sacrificed by focused beam microwave irradn. and amino acids were measured by using a fully validated triple-column ion-exchanged amino acid analyzer with post-column o-phthalaldehyde derivatization and fluorometric detection. The concns. of 4 amino acids, threonine, methionine, lysine, and tyrosine, were increased in 2-4 brain regions by chronic Li+ treatment. Their concns. remained elevated, or were further increased, during status epilepticus. The concns. of 8 amino acids and ammonia were not altered by Li+ treatment but increased in concn. during status epilepticus in some brain regions. Glycine, serine, arginine, and citrulline were decreased by chronic Li+ treatment. Status epilepticus increased the concns. of these 4 amino acids above that found in the Li+-treated samples in some of the brain regions that were examd. Six amino acids and glutathione were generally unaltered by both treatments. These results are related to the effects of Li+ treatment and are compared with changes reported by others following treatment with a variety of **convulsive** stimuli.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, lithium and epilepsy from lithium plus pilocarpine effect on)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



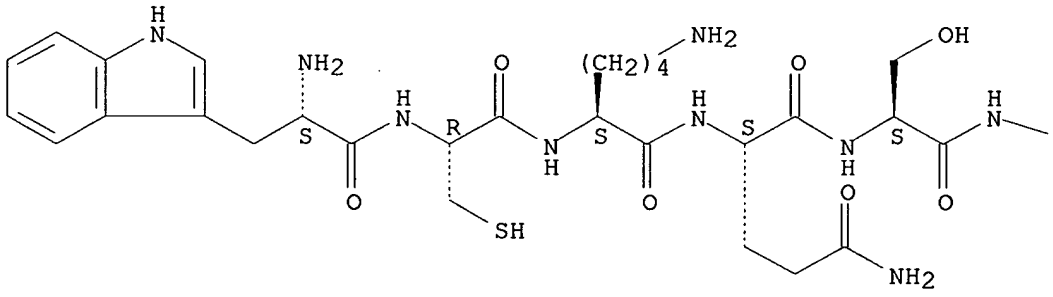
L26 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1989:475819 CAPLUS
DN 111:75819
TI Effect of 2-guanidinoethanol on contents of amino acids in the rat brain
AU Yokoi, Isao; Akiyama, Kenji; Kabuto, Hideaki; Toda, Hiroko; Shimizu, Yoshihisa; Mori, Akitane
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Neurosciences (Okayama, Japan) (1989), 15(1), 35-40
CODEN: NUOCDO; ISSN: 0388-7448
DT Journal; General Review
LA English
AB The contents of amino acids in the rat brain 3 h after the intraventricular injection of 6 .mu.mol of 2-guanidinoethanol (GEt) were measured by HPLC. In the cerebral cortex, glycine and alanine increased significantly. The contents of glutamine, glutamic acid, taurine and aspartic acid did not change in the cerebral cortex, but they decreased in the cerebrum without cerebral cortex. Intraventricularly administered GEt, which is a configurational analog of 4-aminobutanoic acid (GABA), induced twitching, tonic-clonic convulsions and running fits 3 h after the administration, without altering the content of GABA in the rat cerebrum. As GEt blocks the neurotransmission system mediated by GABAA-receptors to induce **convulsive** seizures, changes in the contents of amino acids after GEt administration might be caused by abnormal excitation in the central nervous system.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, guanidinoethanol effect on, pathophysiol. of convulsion in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

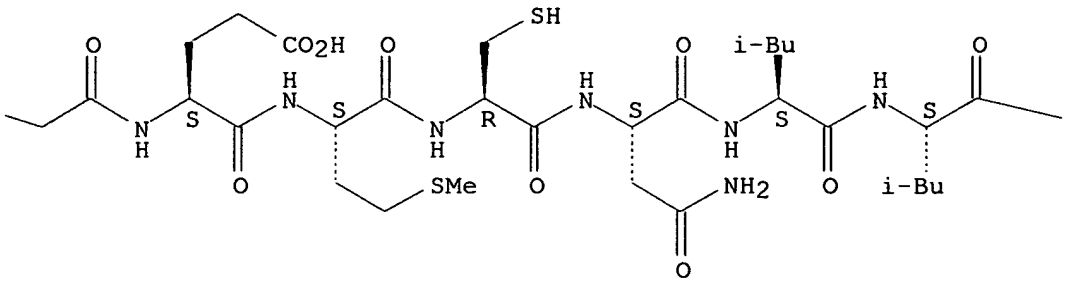
L26 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1989:35520 CAPLUS
DN 110:35520
TI A molluskivorous Conus toxin: conserved frameworks in conotoxins
AU Hillyard, David R.; Olivera, Baldomero M.; Woodward, Scott; Corpuz, Gloria P.; Gray, William R.; Ramilo, Cecilia A.; Cruz, Lourdes J.
CS Mar. Sci. Inst., Univ. Philippines, Manila, Philippines
SO Biochemistry (1989), 28(1), 358-61
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB A 27-amino acid toxin was purified from the venom of the snail-hunting Conus textile and characterized. This toxin causes **convulsivelike** activity in snails and causes subordinate lobsters to assume an exaggerated dominant posture. The sequence of this peptide was detd. directly and was confirmed by detg. the nucleotide sequence of a cDNA clone coding for the peptide. The conservation of cysteine (Cys) residues compared to the .omega.-conotoxins from venom of piscivorous Conus species suggests that toxins from different cone venoms may use only a few Cys-motifs as conserved structural backbones for targeting to a variety of receptors in different animals.
IT **117069-04-2**, Conotoxin King Kong (Conus textile reduced)
RL: PRP (Properties)
(amino acid sequence of)
RN 117069-04-2 CAPLUS
CN .delta.-Conotoxin Tx VIA (reduced) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

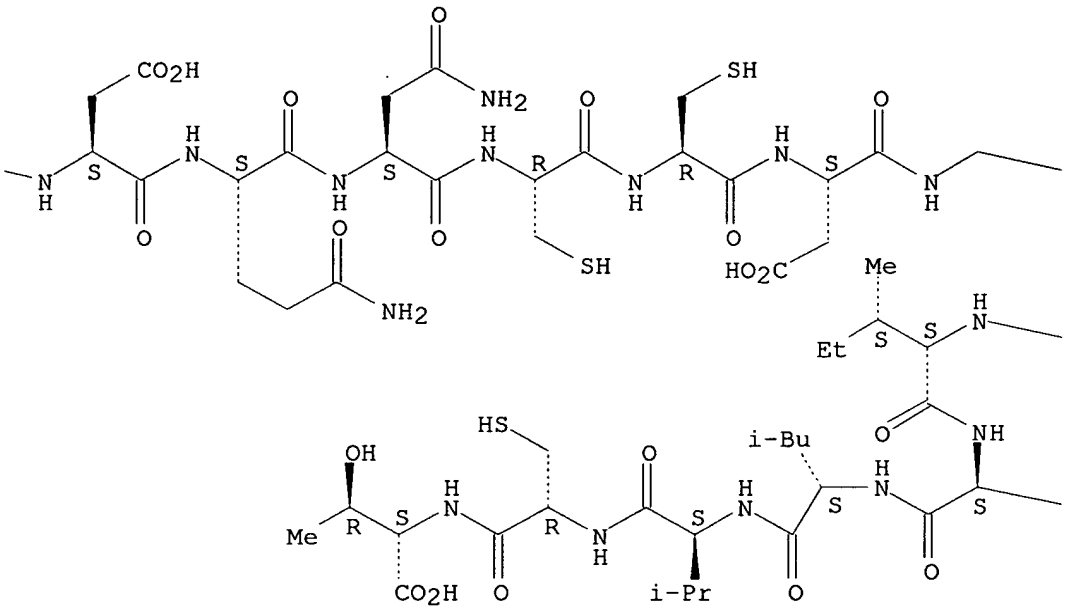
PAGE 1-A



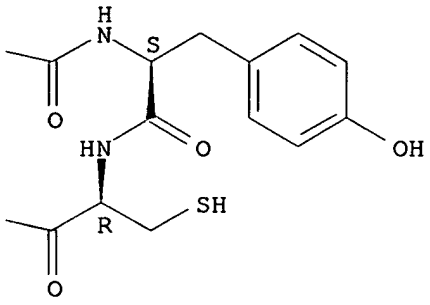
PAGE 1-B



PAGE 1-C

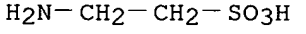


PAGE 1-D

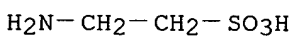


Pr-i

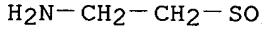
L26 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1988:526843 CAPLUS
DN 109:126843
TI Regional changes in amino acid levels in the brain of El mice due to **convulsive** disposition and seizures
AU Suzuki, Shigeo
CS Sch. Med., Okayama Univ., Okayama, 700, Japan
SO Okayama Igakkai Zasshi (1987), 99(11/12), 1517-28
CODEN: OIZAAV; ISSN: 0030-1558
DT Journal
LA Japanese
AB Amino acid levels were analyzed in the cortex, hippocampus, midbrain, hypothalamus, pons + medulla oblongata, and cerebellum of non-stimulated El mice, El mice stimulated by throwing during the interictal period, and normal ddY mice. Levels of aspartate (Asp), glutamate (Glu), glutamine, and taurine were generally higher in brains of El mice than those of ddY mice. Levels of Asp, Glu, and GABA were lower in the brains of stimulated El mice than those of non-stimulated mice. No difference was found in the hypothalamus. Changes in amino acid levels were examd. during the preconvulsive stage, during convulsions, and after convulsions of stimulated El mice. The Glu level was generally increased during the pre-**convulsive** stage, but the other amino acids were decreased at that time compared with the interictal level. These changes in amino acids were mostly found in the cortex, hippocampus, and midbrain. Glu may play a role in the triggering of seizures in El mice.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain regions, convulsions effect on, in El mice)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1988:524031 CAPLUS
DN 109:124031
TI Effect of guanidinoethanesulfonate and taurine on convulsions in EL mice
AU Hiramatsu, Midori; Edamatsu, Rei; Kabuto, Hideaki; Kuroda, Munemasa; Mori, Akitane
CS Sch. Med., Okayama Univ., Okayama, 700, Japan
SO Ganryu Aminosan (1987), 10(1), 23-6
CODEN: GAMNDY; ISSN: 0387-6667
DT Journal
LA Japanese
AB Mice were given 1% guanidinoethanesulfonate (I) soln. or 1% taurine (II) soln. as drinking water for 6 mo. In the I-treated group, the incidence of convulsions increased throughout the exptl. period from 3 days after starting I treatment as compared with that in the control group. 5-HT contents in the cerebral cortex decreased, whereas those in the caudatum, hippocampus, mesencephalone, hypothalamus, pons + medulla oblongata, and cerebellum showed no change. In the II-treated group, on the other hand, no change was obsd. in the incidence of convulsions or 5-HT contents in each brain area. The levels of brain free amino acids in the I-treated group 3 days after starting of I treatment were measured. Glutamate (Glu), alanine, serine, and lysine (Lys) contents in the cerebrum and Glu, Lys, and glycine contents in the cerebellum increased. The increase in **convulsive** sensitivity to I mice is probably due to both decreased 5-HT levels in the cerebral cortex and increased Glu levels in the brain.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, quanidinoethanesulfonate effect on, convulsions in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



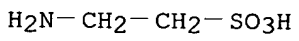
L26 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1988:432566 CAPLUS
DN 109:32566
TI Effect of 5-HTP on brain amino acid levels in E1 mice
AU Hiramatsu, Midori; Edamatsu, Rei; Kuroda, Munemasa
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Neurosciences (Okayama, Japan) (1988), 14(1), 29-35
CODEN: NUOCDO; ISSN: 0388-7448
DT Journal
LA English
AB Inbred mutant E1 mice are highly susceptible to **convulsive** seizures upon throwing stimulation, and reduced 5-HT activity appears to be related to these seizures. To investigate this relation, brain amino acids were analyzed 3 h after administration of 5-HTP (100 mg/kg) with MK486 (10 mg/kg), a dose which completely inhibited the E1 mouse seizures. Taurine level increased and GABA level decreased in the cerebellum but not in the cortex and hippocampus. Other amino acid levels were not changed in the cortex, hippocampus or cerebellum. These results suggest that cerebellar taurine plays a role in the seizure susceptibility of E1 mice.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(in brain cerebellum, hydroxytryptophan effect on, convulsions in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



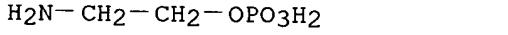
L26 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1988:180744 CAPLUS
DN 108:180744
TI Uptake and release of 5-hydroxytryptamine and taurine in the cerebral cortex of El mice
AU Ogawa, Kazutoshi
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Okayama Igakkai Zasshi (1987), 99(7/8), 751-61
CODEN: OIZAAV; ISSN: 0030-1558
DT Journal
LA Japanese
AB The uptake and release of 5-HT (I) and taurine (II) were examd. in cerebral cortical slices of stimulated and nonstimulated El mice, epileptic mice in which convulsant seizures were easily induced by throwing stimulation, during the intericted period, and were compared with those in ddY mice, the mother strain of El mice devoid of the **convulsive** disposition. Uptake of I and II was lower in stimulated El mice than in nonstimulated El and ddY mice. Release of I and II was higher in nonstimulated El mice than in either ddY or stimulated El mice. No significant difference in spontaneous release of I and II was found among these 3 groups of mice. The level of I in either stimulated or non-stimulated El mice was higher than that in ddY mice, but no significant difference was found between the 2 groups of El mice.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(uptake and release of, by cerebral cortex in epilepsy)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1987:590955 CAPLUS
DN 107:190955
TI The effect of .omega.-phosphono-.alpha.-aminocarboxylic acids on seizures and brain amino acid levels in E1 mice
AU Shimada, Masakatsu; Kabuto, Hideaki; Yokoi, Isao
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Research Communications in Chemical Pathology and Pharmacology (1987), 57(3), 359-73
CODEN: RCOCB8; ISSN: 0034-5164
DT Journal
LA English
AB The effects of .omega.-phosphono-.alpha.-aminocarboxylic acids on seizures and brain amino acids in E1 mice were investigated. These mice are inbred mutant epileptic mice, which are highly susceptible to **convulsive** seizures upon throwing stimulation. 2-Amino-3-phosphonopropionate injected intraventricularly (at a dose of 1.04 .mu.mol) had a marked anticonvulsant action, but at a lower dose (0.1 .mu.mol), it induced running fits. 2-Amino-4-phosphonobutyrate induced transitory excitation just after the injection, followed by sedation. 2-Amino-5-phosphonopentanoate induced marked behavioral sedation. 2-Amino-6-phosphonohexanoate induced tonic-clonic convulsions and epileptic discharges in electroencephalograms. 2-Amino-7-phosphonoheptanoate showed a strong anticonvulsant action at a dose of 1.27 .mu.mol, but it induced myoclonic seizures at a lower dose. Amino acid analyses of E1 mouse brain showed that 2-amino-3-phosphonopropionate increased the glutamine level, 2-amino-4-phosphonobutyrate decreased the aspartic acid level, 2-amino-5-phosphonopentanoate decreased the glutamic acid level, 2-amino-6-phosphonohexanoate decreased the glutamic acid, glutamine, .gamma.-aminobutyric acid, glycine and analine levels, and 2-amino-7-phosphonoheptanoate decreased the glutamic acid label 1 h after their injection. Apparently, the effects of .omega.-phosphono-.alpha.-aminocarboxylic acids on the E1 mouse brain are multiple and complicated, depending on the nos. of their carbon chain.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, phosphonoaminocarboxylic acids effect on, in mouse epilepsy model)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



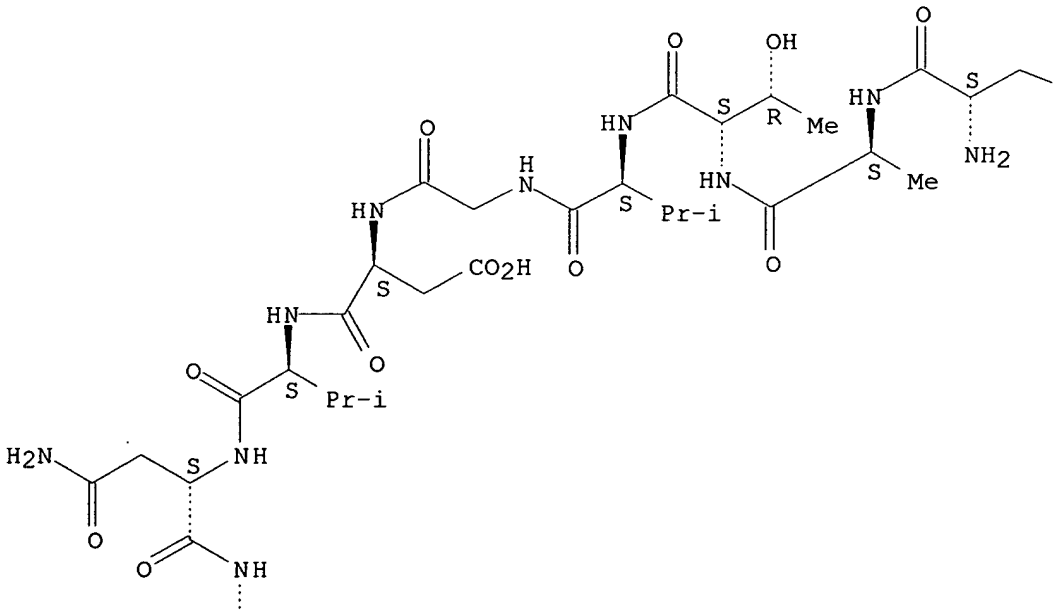
L26 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1987:437540 CAPLUS
DN 107:37540
TI Cerebellar metabolism of phosphatidylethanolamine and its water-soluble precursors during bicuculline-induced **convulsive** seizures
AU Marku, Ndok; Corazzi, Lanfranco; Piccinin, Gian Luigi; Arienti, Giuseppe
CS Med. Sch., Univ. Perugia, Perugia, 06100, Italy
SO Neurochemical Research (1987), 12(4), 341-4
CODEN: NEREDZ; ISSN: 0364-3190
DT Journal
LA English
AB The incorporation of labeled ethanolamine into phosphatidylethanolamine (PE) and its water-sol. precursors, phosphoethanolamine and CDP-ethanolamine, was measured in rat cerebella during the course of bicuculline-induced **convulsive** seizures. The labeling of CDP-ethanolamine and phosphoethanolamine diminished 6 min after the administration of both bicuculline and radioactive ethanolamine, whereas that of PE was unaffected in these conditions. Time was very important to this effect; indeed, no differences of the labeling of PE water-sol. precursors could be found in rat cerebellum of normal and convulsing animals 12 min after the administration. The cerebellar pool of CDP-ethanolamine doubled after 6 min of convulsions, which means that unlabeled CDP-ethanolamine forms from a non-radioactive source, such as lipid, maybe through the reversal of the ethanolamine phosphotransferase reaction. This effect disappears 12 min after the injection of the convulsant.
IT **1071-23-4**, Phosphoethanolamine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of, by cerebellum in bicuculline-induced convulsions)
RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)



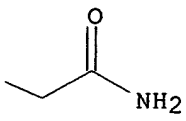
L26 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1987:150223 CAPLUS
DN 106:150223
TI Octadecaneuropeptide (ODN; 'anxiety peptide') displaces diazepam more potently from astrocytic than from neuronal binding sites
AU Bender, Alexander S.; Hertz, Leif
CS Dep. Pharmacol., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SO European Journal of Pharmacology (1986), 132(2-3), 335-6
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB Anxiety peptide [**95237-86-8**], an octadecaneuropeptide component of the polypeptide diazepam binding inhibitor, inhibited the binding of 3H-labeled diazepam [439-14-5] by primary cultures of mouse astrocytes and cerebral cortical neurons. The astrocyte cultures were the most sensitive, with median inhibitory concn. (IC50) values of the octadecaneuropeptide being 142 nM and 6.7 .mu.M for astrocytes and neurons, resp. Thus, astrocytic benzodiazepine receptors are apparently involved in mediating the anxiogenic and **convulsive** effects of the octadecaneuropeptide. Consequently, such receptors may be involved in anxiety disorders and **convulsive** states.
IT **95237-86-8**
RL: BIOL (Biological study)
(benzodiazepine receptors of astrocytes affinity for)
RN 95237-86-8 CAPLUS
CN L-Lysine, L-glutaminyl-L-alanyl-L-threonyl-L-valylglycyl-L-.alpha.-aspartyl-L-valyl-L-asparaginyl-L-threonyl-L-.alpha.-aspartyl-L-arginyl-L-prolylglycyl-L-leucyl-L-leucyl-L-.alpha.-aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

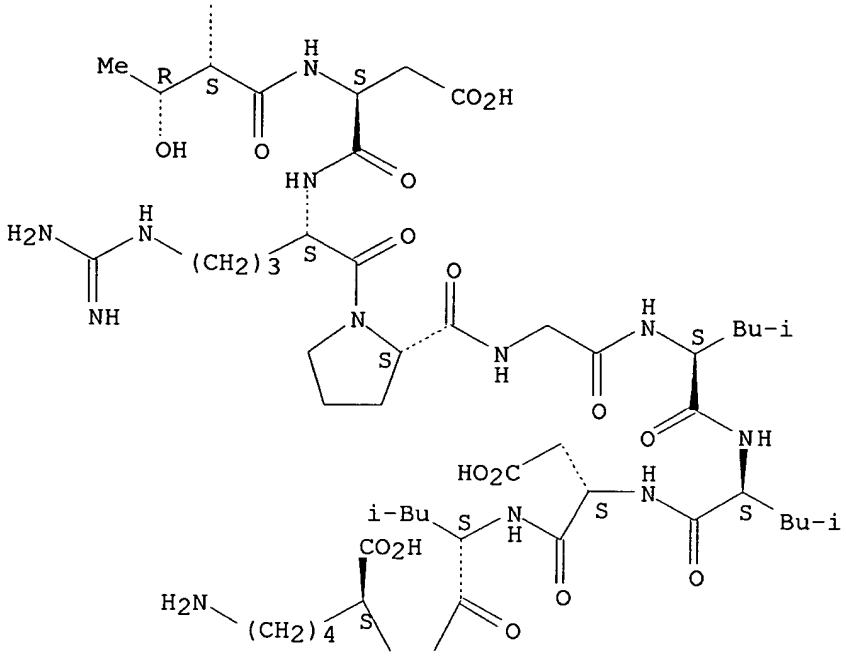
PAGE 1-A



PAGE 1-B



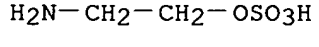
PAGE 2-A



PAGE 3-A

L26 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1987:117513 CAPLUS
DN 106:117513
TI Reduced uptake and release of 5-hydroxytryptamine and taurine in the cerebral cortex of epileptic El mice
AU Hiramatsu, Midori; Ogawa, Kazutoshi; Kabuto, Hideaki; Mori, Akitane
CS Med. Sch., Okayama Univ., Okayama, 700, Japan
SO Epilepsy Research (1987), 1(1), 40-5
CODEN: EPIRE8; ISSN: 0920-1211
DT Journal
LA English
AB Inbred mutant El mice are highly susceptible to **convulsive** seizures upon 'throwing' stimulation, and the inhibition of 5-hydroxytryptamine (5-HT) and taurine activities appears to be involved in the El mouse seizures. Uptake and release of [3H]5-HT and [3H]taurine into and from cerebral neurocortical slices using a superfusion system were investigated in both non-stimulated and stimulated El mice [El(-), El(+)] and in ddY mice, which do not have a **convulsive** disposition. Release was defined as 40 mM K+-stimulated release. 5-HT and taurine uptake in El(+) was lower than El(-) but no difference in either uptake was found between ddY and El(-). Release of 5-HT and taurine in El(-) was higher than in ddY whereas their release in El(+) was lower than in El(-). The taurine level in the cerebral neocortex of El(-) and El(+) was higher than in ddY. Apparently, the synaptic function of the 5-HT and taurine contg. neurons is suppressed and dysfunction of these inhibitory neurons is involved in the seizure susceptibility in the El mice.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(uptake and release of, by brain in epilepsy in El mouse)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

L26 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1985:215127 CAPLUS
DN 102:215127
TI The modulation of cortical acetylcholine release by GABA, GABA-like drugs and benzodiazepines in freely moving guinea pigs
AU Tanganelli, S.; Bianchi, C.; Beani, L.
CS Dep. Pharmacol., Univ. Ferrara, Ferrara, 44100, Italy
SO Neuropharmacology (1985), 24(4), 291-9
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB In order to define the modulatory role played by GABA [56-12-2] in corticopetal cholinergic projections, the effect of this amino acid and related drugs on gross behavior, the EEG and the release of acetylcholine (ACh) [51-84-3] from the cerebral cortex in freely moving guinea pigs was studied. GABA, injected intracerebroventricularly (20-50 .mu.mol), induced a 3-phase picture: first (5-15 min) behavioral activation and increased release of ACh, then (30-90 min) depression, EEG synchronization and reduced release of ACh, and finally "rebound" stimulation. Ethanolamine-O-sulfate [**926-39-6**] injected intraventricularly (28 .mu.mol/kg) or i.p. (14 mmol/kg) reproduced the first 2 phases of the effects of GABA (i.e. stimulation followed by inhibition), while diazepam [439-14-5] (0.7 and 3.5 .mu.mol/kg, i.p.) and flurazepam [17617-23-1] (32 .mu.mol/kg, i.p.) caused, at first, only depression. Muscimol [2763-96-4] and THIP [64603-91-4] injected intraventricularly (in the nmol range) or i.p. (in the .mu.mol range) produced behavioral activation and increased release of ACh; the depressant signs appeared only after very large, toxic doses. Picrotoxin [124-87-8] and bicuculline [485-49-4], at sub-**convulsive** doses, reduced the symptomatol. caused by GABA and antagonized the sedation produced by diazepam. Methylsergide [361-37-5] (8-16 .mu.mol/kg, i.p.) prevented the behavioral activation and the increased release of ACh by GABA, unmasked the depression due to subthreshold doses of diazepam (intraventricularly, 7-70 nmol) and reversed the stimulation induced by muscimol into sedation and reduced the outflow of ACh. Pretreatment with 5,7-dihydroxytryptamine [31363-74-3] also dampened and shortened the stimulation by muscimol. Apparently, compds. related to GABA interact sequentially and/or preferably with two subtypes of conventional GABA receptors, differing in their functional role. Benzodiazepines mainly facilitate GABA-mediated inhibitory mechanisms, also involving cholinergic neurons, while muscimol and THIP, interact with GABA recognition sites, which restrain tryptoaminergic neurons, thus detg. behavioral and cholinergic disinhibition. The interrelationship of these opposite effects explains the complex pattern of effects of exogenous GABA and ethanolamine-O-sulfate and accounts for the different influences exerted by GABA-like compds. in the physiol. disposition of ACh in various animal species and areas of the brain.
IT **926-39-6**
RL: BIOL (Biological study)
(acetylcholine release by brain cerebral cortex response to, behavior and EEG response in)
RN 926-39-6 CAPLUS
CN Ethanol, 2-amino-, hydrogen sulfate (ester) (8CI, 9CI) (CA INDEX NAME)



L26 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1985:199073 CAPLUS
DN 102:199073
TI Effects of glycine and other inhibitory amino acid neurotransmitters on strychnine **convulsive** threshold in mice
AU Sangiah, Subbiah
CS Coll. Vet. Med., Oklahoma State Univ., Stillwater, OK, 74078, USA
SO Veterinary and Human Toxicology (1985), 27(2), 97-9
CODEN: VHTODE; ISSN: 0145-6296
DT Journal
LA English
AB The effects of glycine [56-40-6] and other inhibitory amino acid neurotransmitters on strychnine (I) [57-24-9] **convulsive** threshold were studied in mice. The mean i.v. threshold dose for I to produce its **convulsive** effects in briefly restrained mice was 1386 mg/kg. The dose of I produced 100% postconvulsive mortality in all the mice tested. I.p. administration of various doses (100-500 mg/kg) of glycine, .beta.-alanine [**107-95-9**], and L-threonine [72-19-5], 15-20 min prior to I infusion, produced an increase of 13.92%, 25.73% and 17.15%, resp., in I **convulsive** threshold in mice. Diazepam [439-14-5], known to produce its anticonvulsant, sedative, and muscle relaxant effects through its interaction either with central GABA or glycine receptors was the most potent (48.39%) in increasing I **convulsive** threshold. Laurine [107-75-5] and Baclofen [1134-47-0] were ineffective in raising I **convulsive** threshold in mice. These observations favor the possible use of either glycine or .beta.-alanine in addn. to diazepam in treating clin. cases of I neurotoxicoses.
IT **107-35-7 107-95-9**
RL: BIOL (Biological study)
(strychnine-induced **convulsive** threshold response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

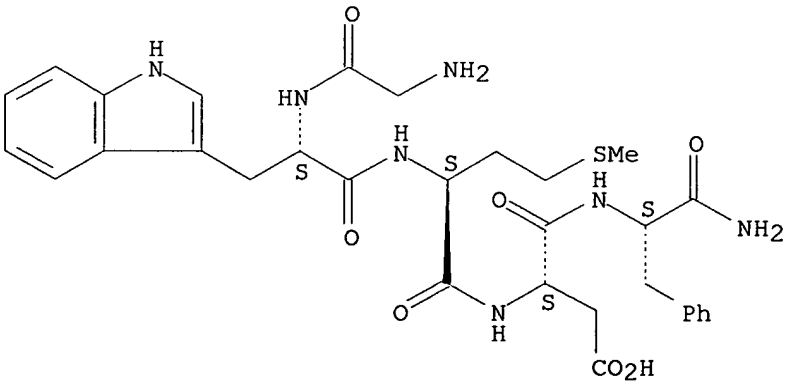
$H_2N-CH_2-CH_2-SO_3H$

RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

L26 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1985:179251 CAPLUS
DN 102:179251
TI Effects of cholecystokinin octapeptides and their fragments on seizures induced by different **convulsive** drugs
AU Kadar, T.; Pesti, A.; Toth, G.; Penke, B.; Telegdy, G.
CS Dep. Pathophysiol., Univ. Med. Sch., Szeged, Hung.
SO Neuropept. Psychosom. Processes, Int. Conf. Integr. Neurohumoral Mech. (1983), Meeting Date 1982, 231-8. Editor(s): Endroczi, Elember. Publisher: Akad. Kiado, Budapest, Hung.
CODEN: 53HNAO
DT Conference
LA English
AB The antagonist activities of cholecystokinin octapeptide sulfate ester (CCK-8-SE) [25126-32-3], nonsulfated cholecystokinin octapeptide (CCK-8-NS) [25679-24-7] and fragments of these mols. on **convulsive** seizures induced by pentetrazole [54-95-5], strychnine [57-24-9], and picrotoxin [124-87-8] were examd. in mice and rats. Peptides were administered i.p. to mice and intracerebroventricularly to rats, 10 min before administration of the convulsant drug. CCK-8-SE and CCK-8-NS antagonized picrotoxin-induced seizures in both mice and rats, but had no effect on strychnine and pentetrazole-induced convulsions. In both species the octapeptide fragments which attenuated picrotoxin-induced seizures or prolonged the time until death contained the C-terminal tetrapeptide amide (CCK-5-8 [1947-37-1]) sequence of the mol. The C-terminal tripeptide (CCK-6-8 [5934-92-9]) and dipeptide (CCK-7-8 [5241-71-4]) had no anticonvulsive activity. The N-terminal nonsulfated tetrapeptide (CCK-1-4-NS [80790-40-5]) also slightly antagonized the effect of picrotoxin, but only in rats.
IT **18917-24-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, structure in relation to)
RN 18917-24-3 CAPLUS
CN 3-7-Cholecystokinin-7 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



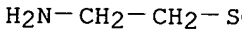
L26 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1984:628789 CAPLUS
DN 101:228789
TI Subcellular distribution of neuroactive amino acids in brains of genetically epileptic rats
AU Bonhaus, Douglas W.; Lippincott, Shirley E.; Huxtable, Ryan J.
CS Health Sci. Cent., Univ. Arizona, Tucson, AZ, USA
SO Epilepsia (1984), 25(5), 564-8
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB The subcellular distribution of amino acids was compared in brains of genetically seizure-susceptible (SS) and genetically seizure-resistant (SR) rats. The total taurine content (.mu.mol/brain) in the P2B, or synaptosomal, fraction in SS rats was only 37% of that of SR rats. Glutamate, glutamine, glycine, alanine, and GABA contents were unaltered. No alterations in total content were found in other subcellular fractions of the amino acids studied. SS animals that had never been stimulated to audiogenic seizure had decreased concns. of taurine (nmol/mg protein) in the P2, P2B, and P2C fractions as compared with SR animals. These fractions contain crude synaptosomes, enriched synaptosomes, and enriched mitochondria, resp. Phosphoethanolamine concns. were also decreased in the P2B fractions, but concns. of other amino acids were unaltered, as compared with SR animals. Twenty-four hours after the intracerebroventricular injection of taurine (6 .mu.mol) in SS animals that had never been convulsed, taurine concns. were increased in whole-brain homogenate and P2 and P2B fractions as compared with SS not given taurine. This treatment left unaltered the concns. of glutamate, glutamine, GABA, and glycine in brain homogenate and P2 fraction. Because decreases in taurine concn. were seen in animals that had not been convulsed, these alterations are intrinsic to the SS strain and are not a consequence of **convulsive** activity. In view of the antiepileptic action of taurine, and the fact that an impairment of taurine transport in the brain of SS rats has previously been demonstrated, it is suggested that a defect in the biochem. of taurine is partially responsible for the seizure susceptibility of the SS rat.
IT **107-35-7 1071-23-4**
RL: PROC (Process)
(brain subcellular distribution of, in genetic epilepsy susceptibility)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-OPO_3H_2$

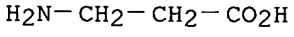
L26 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1983:516696 CAPLUS
DN 99:116696
TI Participation of GABA and other transmitters in **convulsive** threshold regulation
AU Georgiev, V. P.
CS Inst. Fiziol., Sofia, Bulg.
SO Farmakologiya i Toksikologiya (Moscow) (1983), 46(4), 15-19
CODEN: FATOAO; ISSN: 0014-8318
DT Journal
LA Russian
AB The participation of GABA [56-12-2] and some other neurotransmitter systems in the regulation of the **convulsive** seizure threshold was studied in mice in which convulsions were induced by the GABA antagonists picrotoxin and bicuculline or, in some cases, by pentylenetetrazole and strychnine. GABA injected intracerebroventricularly increased the **convulsive** seizure threshold of i.v. picrotoxin at doses as low as 0.2 nmol; glycine [56-40-6] and taurine [**107-35-7**] also increased it but only at 200 nmol. The **convulsive** seizure threshold was also increased by cholinomimetics, dopamine agonists, serotonin [50-67-9], benzodiazepines, and cyclic nucleotides, indicating interactions between GABAergic, cholinergic, dopaminergic, and serotoninergic mechanisms, benzodiazepine receptors, and cyclic nucleotides in **convulsive** threshold regulation. The changes in the threshold of **convulsive** reactions were closely related to the decrease or increase of central inhibition (pre- or postsynaptic) and excitation.
IT **107-35-7**
RL: BIOL (Biological study)
(convulsion threshold enhancement by)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



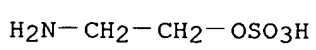
L26 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1982:1232 CAPLUS
DN 96:1232
TI Effect of taurine on seizures induced by 4-aminopyridine
AU Pasantes-Morales, H.; Arzate, M. E.
CS Cent. Invest. Fisiol. Cel., Univ. Nac. Auton. Mexico, Mexico City, Mex.
SO Journal of Neuroscience Research (1981), 6(4), 465-74
CODEN: JNREDK; ISSN: 0360-4012
DT Journal
LA English
AB The effect of i.p. injected taurine [**107-35-7**] against the **convulsive** activity induced by 4-aminopyridine (4-AP) [504-24-5] was studied in 12-15-day-old mice. At a dose of 2.6 mg/kg, taurine increased the latency of clonic seizures from 7 to 20 min, reduced the incidence of tonic seizures from 92 to 30% and the postconvulsive mortality from 80 to 31%. The injection of EDTA prior to the administration of taurine prevented the protective effect of the amino acid. GABA and glycine at the same doses did nt protect against 4-AP-induced seizures. 4-AP caused a small increase (19%) in 45Ca accumulation by mice brain synaptosomes incubated in a Krebs-HEPES medium contg. low CaCl2 (0.1 mM) and also slightly potentiated the veratrine and K-induced increase in Ca accumulation. 4-AP at concns. of 1-2 mM caused a marked increase (100-500%) of 45Ca accumulation by synaptosomes incubated in a Krebs-bicarbonate medium contg. 2.5 mM CaCl2. This increase was completely antagonized by taurine but not by GABA or glycine. The anticonvulsant effect of taurine might be mediated by 4-AP-Ca-taurine interactions.
IT **107-35-7**
RL: BIOL (Biological study)
(aminopyridine-induced convulsions inhibition by, calcium in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1981:154190 CAPLUS
DN 94:154190
TI Sensitivity of identified medial hypothalamic neurons to GABA, glycine and related amino acids; influence of bicuculline, picrotoxin and strychnine on synaptic inhibition
AU Blume, H. W.; Pittman, Q. J.; Renaud, L. P.
CS Montreal Gen. Hosp., McGill Univ., Montreal, QC, H3G 1A4, Can.
SO Brain Research (1981), 209(1), 145-58
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Medial hypothalamic neurons in pentobarbital anesthetized rats were identified by location and response to elec. stimulation of the amygdala, medial preoptic area, midbrain periaqueductal gray and median eminence. Cells were then examd. for their sensitivity to microiontophoretic applications of GABA [56-12-2], glycine [56-40-6] and 3 related amino acids, i.e. .beta.-guanidinopropionic acid [353-09-3], .delta.-aminovaleric acid [660-88-8] and .beta.-alanine [**107-95-9**]. Application of all agents decreased the spontaneous and glutamate or aspartate evoked activity of the majority of neurons in all identified categories. The majority of neurons were more sensitive to .beta.-guanidinopropionate, .delta.-aminovalerate and GABA than to glycine and .beta.-alanine. Bicuculline-HCl [28002-61-1] and picrotoxin [124-87-8] produced a selective and reversible antagonism of depressions evoked by GABA and GABA-like amino acids whereas strychnine sulfate [60-41-3] produced a selective and reversible antagonism of depressions evoked by glycine and .beta.-alanine. Bicuculline and picrotoxin, but not strychnine, were obsd. to diminish synaptic inhibition evoked by elec. stimulation of several sites when these agents were administered by microiontophoresis and by i.v. injections in **convulsive** doses. Apparently, medial hypothalamic neurons have both GABA and glycine receptors but GABA may have the more important role as a neurotransmitter common to afferent or recurrent inhibitory hypothalamic pathways.
IT **107-95-9**
RL: BIOL (Biological study)
(hypothalamus neurons sensitivity to)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



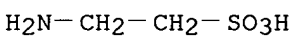
L26 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1981:132942 CAPLUS
DN 94:132942
TI A comparative study of the pharmacology of inhibitors of GABA-metabolism
AU Loescher, Wolfgang
CS Fachber. Veterinaermed., Freie Univ. Berlin, Berlin, D-1000/33, Fed. Rep. Ger.
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1980), 315(2), 119-28
CODEN: NSAPCC; ISSN: 0028-1298
DT Journal
LA English
AB Gabaculine [59556-29-5], .gamma.-acetylenic GABA [57659-38-8], .gamma.-vinyl GABA [60643-86-9], ethanolamine O-sulfate (EOS) [**926-39-6**], aminooxyacetic acid hemihydrochloride (AOAA) [2921-14-4], Na valproate (VPA) [1069-66-5], and GABA [56-12-2] were studied for anticonvulsant, biochem. and toxic effects in mice. Elevations of the electroconvulsive threshold were produced by the i.p. injection of AOAA, gabaculine, .gamma.-acetylenic GABA, VPA, EOS, .gamma.-vinyl GABA and GABA in decreasing order of potency. All drugs except GABA and VPA increased the clonic pentetrazole threshold to a similar extent, but differed in their increases in the brain content of GABA. The activity of glutamate decarboxylase [9024-58-2]was decreased only by .gamma.-acetylenic GABA. Gabaculine, AOAA, VPA, and in part .gamma.-vinyl GABA and GABA were efficacious enough to allow the detn. of anticonvulsant ED50 values, whereas .gamma.-acetylenic GABA and EOS showed no clear activity in any seizure models used. Gabaculine and AOAA were toxic or lethal. All inhibitors of GABA-.alpha.-oxoglutarate aminotransferase (EC 2.6.1.19) (GABA-T) [9037-67-6]xcept EOS caused numerous side effects which cast doubt on the specificity of these drugs. Apparently, inhibitors of GABA-T are not suited for treatment of **convulsive** disorders in humans but are useful tools in studies of exptl. epilepsy.
IT **926-39-6**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pharmacol. and toxicity of)
RN 926-39-6 CAPLUS
CN Ethanol, 2-amino-, hydrogen sulfate (ester) (8CI, 9CI) (CA INDEX NAME)



L26 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1980:34386 CAPLUS
DN 92:34386
TI Effect of taurin on audiogenic **convulsive** fits in rats
AU Batuev, A. S.; Ryabinskaya, E. A.; Gudimova, N. V.
CS Leningr. Gos. Univ., Leningrad, USSR
SO Doklady Akademii Nauk SSSR (1979), 248(6), 1496-9 [Physiol.]
CODEN: DANKAS; ISSN: 0002-3264
DT Journal
LA Russian
AB The i.p. injection of 1.0-1.2 g taurine [**107-35-7**]/kg decreased in rats the incidence and severity of audiogenically induced convulsions. The effect persisted for .apprx.10 days.
IT **107-35-7**
RL: BIOL (Biological study)
(audiogenic convulsions response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

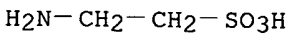
$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1979:450076 CAPLUS
DN 91:50076
TI Effects of taurine, glycine and GABA on convulsions produced by strychnine in the rabbit
AU Roches, J. C.; Zumstein, H. R.; Faessler, A.; Scollo-Lavizzari, G.; Hoesli, L.
CS Neurol. Clin., Univ. Basel, Basel, Switz.
SO European Neurology (1979), 18(1), 26-32
CODEN: EUNEAP; ISSN: 0014-3022
DT Journal
LA English
AB The action of injected taurine [**107-35-7**], glycine [56-40-6], and GABA [56-12-2] on convulsions induced by strychnine (I) [57-24-9], was tested using electroencephalog. recordings. The dose of I necessary to produce a generalized tonic-clonic seizure was 0.55 mg/kg, i.v. for rabbits pretreated with taurine, which was higher than for control animals (0.38 mg/kg). After pretreatment with glycine, the I dose required to evoke convulsions (0.51 mg/kg) was also higher than the control values, but the difference was not significant. The **convulsive** dose of I in animals pretreated with GABA was slightly but not significantly lower than in control animals (0.31 mg/kg). Apparently, taurine is the most effective amino acid to protect rabbits from seizures induced by I.
IT **107-35-7**
RL: BIOL (Biological study)
(strychnine-induced convulsions response to, in rabbit)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



File Copy

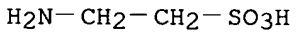
L26 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1978:470974 CAPLUS
DN 89:70974
TI The prolonged anticonvulsant action of taurine on genetically determined seizure-susceptibility
AU Huxtable, R.; Laird, H.
CS Dep. Pharmacol., Univ. Arizona, Tucson, AZ, USA
SO Canadian Journal of Neurological Sciences (1978), 5(2), 215-21
CODEN: CJNSA2; ISSN: 0317-1671
DT Journal
LA English
AB A prolonged anticonvulsant action of taurine [**107-35-7**] was shown in a strain of seizure susceptible rats. The audiogenic rat (AS) had lower intracerebral electroshock thresholds in 3 auditory nuclei; the ventral cochlear, the inferior colliculi and the medial geniculate, and in 1 nonauditory structure; the reticular formation, than a strain of nonaudiogenic rats (NAS). Furthermore, the AS animals routinely displayed more maximal (tonic-clonic) convulsion, regardless of brain structure stimulated, whereas NAS subjects responded with minimal (clonic) convulsions. Within 3 minutes of intraventricular injection of 8 .mu. moles, taurine decreased the susceptibility of AS rats to intracerebral electroshock seizures along with attenuation of the severity of the convulsion. The inital elevation in intracerebral electroshock threshold returned to pretreatment value at 24 h, only to rise again at 48 h and to remain elevated through day 6 after injection. In contrast, the severity of convulsions remained attenuated through 24 h, after which it returned to preinjection level. By comparison, NAS animals injected intracerebroventricularly in an identical fashion to the AS rats showed no changes in either seizure threshold or severity of convulsion. The direct injection of 200 nmoles of taurine in the inferior colliculi of AS rats produced a slow developing, but prolonged, elevation of intracerebral electroshock threshold of this auditory nuclei. However, at no time after the intracerebral injection of taurine was **convulsive** severity changed. Injection of taurine into the inferior colliculi of NAS subjects did not change either susceptibility or severity of intracerebral electroshock seizures. Thus, taurine appears to produce an anticonvulsant effect which is slow in onset, potent, selective and prolonged.
IT **107-35-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1978:456973 CAPLUS
DN 89:56973
TI Microdistribution of taurine and cysteine sulfinate decarboxylase activity in rat spinal cord and thalamus: Comparison with .gamma.-aminobutyric acid and L-glutamic acid decarboxylase
AU Kuriyama, Kinya; Yoneda, Yukio; Kurihara, Etsuo
CS Dep. Pharmacol., Kyoto Prefect. Univ. Med., Kyoto, Japan
SO Taurine Neurol. Disord., [Symp.] (1978), Meeting Date 1977, 35-48. Editor(s): Barbeau, Andre; Huxtable, Ryan J. Publisher: Raven, New York, N. Y.
CODEN: 38JDAH
DT Conference
LA English
AB In horizontal sections of rat spinal cord, taurine was rather evenly distributed, whereas the GABA levels and the cysteine sulfinate decarboxylase (I) and L-glutamic acid decarboxylase (II) activities were higher in the dorsal half than in the ventral half. Both taurine and I were evenly distributed in rat thalamus sections at 5.4 mm anterior to the interaural line, whereas GABA and II were unevenly distributed. Morphine administration markedly increased GABA levels in the dorsal horn and around the central canal of the spinal cord and increased GABA and II levels in only certain regions of the thalamus, but did not significantly alter the taurine and I distributions. **Convulsive** doses of strychnine also did not alter taurine and I distributions. A neurotransmitter role for taurine in the thalamus and spinal cord is not indicated.
IT **107-35-7**
RL: PROC (Process)
(of brain thalamus and spinal cord, distribution of)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L26 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1978:437333 CAPLUS
DN 89:37333
TI Interrelations between inhibitory amino acids and **convulsive** neurostimulants at the **convulsive**-seizure threshold
AU Georgiev, V.; Petkova-Radkova, B.
CS Sect. Pharmacol., Inst. Physiol., Sofia, Bulg.
SO Doklady Bolgarskoi Akademii Nauk (1977), 30(12), 1795-8
CODEN: DBANAD; ISSN: 0366-8681
DT Journal
LA English
AB The effects of intracerebroventricular pretreatment (15 or 30 min) on mice with equimolar concns. of the inhibitory transmitter Reanal (GABA) [56-12-2], glycine [56-40-6], and taurine [**107-35-7**] on the **convulsive** thresholds of i.v. administered strychnine nitrate [66-32-0], bicucullin [485-49-4], picrotoxin [124-87-8], and Tetracor (pentylenetetrazole) [54-95-5] were studied. The **convulsive** thresholds of both picrotoxin and bicucullin were increased by all the 3 amino acids; GABA (200 .mu.mol/mouse) had the strongest effect (72% increase) on picrotoxin **convulsive** threshold while bicucullin **convulsive** threshold was increased maximally by taurine (200 .mu.mol/mouse). Pentylenetetrazole **convulsive** threshold was increased only slightly by all the 3 inhibitory transmitters. While GABA (200 .mu.mol/mouse) increased the strychnine **convulsive** threshold, glycine (all dose levels), and taurine (20 .mu.mol/mouse) decreased the threshold; at 200 .mu.mol/mouse taurine increased the strychnine **convulsive** threshold slightly when applied 30 min before strychnine administration. Thus, when directly applied to the brain, GABA, glycine, and taurine do not show similar effects against stimulant-induced convulsion.
IT **107-35-7**
RL: PRP (Properties)
(**convulsive** threshold of neurostimulants response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1975:119543 CAPLUS
DN 82:119543
TI Effect of the **convulsive** agent 3-mercaptopropionic acid on the levels of GABA, other amino acids, and glutamate decarboxylase in different regions of the rat brain
AU Karlsson, Arve; Fonnum, Frode; Malthe-Soerenssen, Didrik; Storm-Mathisen, Jon
CS Div. Toxicol., Norw. Def. Res. Estab., Kjeller, Norway
SO Biochemical Pharmacology (1974), 23(21), 3053-61
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB Concomitant decreases in brain GABA (I) [56-12-2] levels and glutamate decarboxylase (EC 4.1.1.15) (II) [9024-58-2] activity were obsd. prior to convulsions induced by 3-mercaptopropionic acid [107-96-0], suggesting that convulsions are caused by a redn. of I concn. by inhibition of II. Aspartate [56-84-8] and taurine [**107-35-7**] levels were decreased in all brain regions during convulsions. The **convulsive** agent did not inhibit the uptake of I into synaptosomes.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, convulsion effect on)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

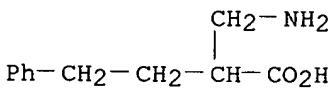
=> d l28 1-11 bib,ab,hitstr

L28 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:716608 CAPLUS
DN 137:242191
TI Antiepileptogenic agents
IN Weaver, Donald F.; Tan, Christopher Y. K.; Kim, Stephen T.; Kong, Xianqi; Wei, Lan; Carran, John R.
PA Queen's University at Kingston, Can.; Neurochem Inc.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002073208	A2	20020919	WO 2002-CA363	20020313

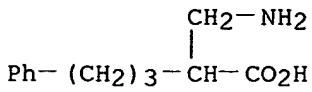
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-275618P P 20010313
OS MARPAT 137:242191
AB The invention discloses methods and compds. useful for the **treatment** of **convulsive** disorders, including epilepsy. The methods and compds. of the invention inhibit or prevent ictogenesis and/or epileptogenesis. The invention also discloses methods for prepg. these anticonvulsant compds.
IT **460039-38-7 460039-39-8 460039-44-5 460039-45-6**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-epileptogenic agents)
RN 460039-38-7 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

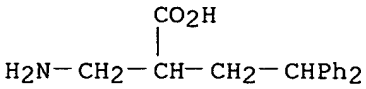


● HCl

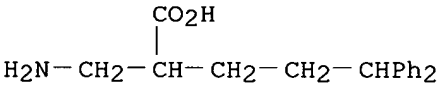
RN 460039-39-8 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



RN 460039-44-5 CAPLUS
CN Benzenebutanoic acid, .alpha.-(aminomethyl)-.gamma.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

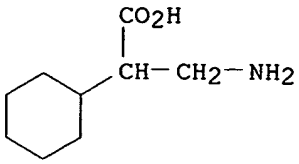


RN 460039-45-6 CAPLUS
CN Benzenepentanoic acid, .alpha.-(aminomethyl)-.delta.-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

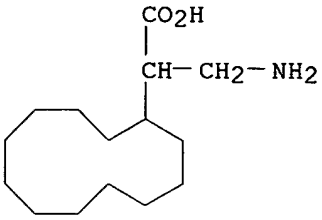


IT **107-95-9D**, .beta.-Alanine, esters
RL: PAC (Pharmacological activity); BIOL (Biological study)
(anti-epileptogenic agents)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

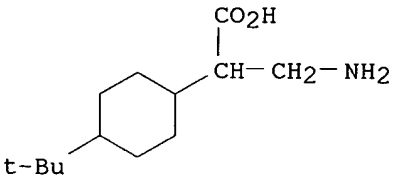
IT **5664-30-2P 213192-16-6P 213192-49-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-epileptogenic agents)
RN 5664-30-2 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)

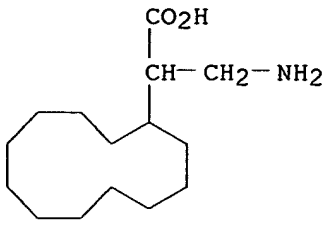


RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **213192-76-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(anti-epileptogenic agents)
RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L28 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2000:34961 CAPLUS
DN 132:73661
TI Cells and animals deficient in the .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics
IN Messing, Robert O.; Hodge, Clyde W.
PA USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000001805	A1	20000113	WO 1999-US15152	19990702
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002124272	A1	20020905	US 1999-340283	19990625
	AU 9949689	A1	20000124	AU 1999-49689	19990702
	EP 1095136	A1	20010502	EP 1999-933688	19990702
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	JP 2002522012	T2	20020723	JP 2000-558195	19990702
	ZA 2000007494	A	20020415	ZA 2000-7494	20001214
	ZA 2000007780	A	20020322	ZA 2000-7780	20001221
	US 2002151465	A1	20021017	US 2002-39278	20020104
PRAI	US 1998-91755P	P	19980706		
	US 1999-125995P	P	19990324		
	US 1999-340283	A	19990625		
	US 1998-91755	P	19980706		
	US 1998-103763P	P	19981009		
	US 1999-125995	P	19990324		
	WO 1999-US15152	W	19990702		
	US 1999-347370	A1	19990706		

AB Cells and animals deficient in protein kinase C .epsilon. isoenzyme (PKC.epsilon.) that can be used to screen for anti-anxiety drugs are described. According to the present invention, PKC.epsilon.-inhibiting compds. act in synergy with drugs acting at the GABAA receptor. These modulators of PKC.epsilon. may also be used to modulate alc. consumption, self-administration of other drugs of abuse, and the effects of alc. consumption. PKC.epsilon. inhibitors may also also be used either alone or in conjunction with allosteric agonists of GABAA receptors, to **treat** conditions, such as addiction, withdrawal syndrome, skeletal muscle spasms, **convulsive** seizures, and epilepsy, that are amenable to **treatment** by allosteric agonists of GABAA receptors. Addnl. aspects of the present invention are diagnostic methods for identifying individuals at risk for becoming alcoholics or abusers of other drugs and kits for performing such diagnostic methods. Transgenic homozygous PKC.epsilon. knockout mice were found to show lower levels of anxiety than control animals. Gross anatomy of the knockout mice is essentially normal, but there are changes in the patterns of fiber

outgrowth and branching in the stratum radiatum. The knockout mice showed lower levels of alc. consumption in ethanol preference drinking tests with a 75% lowering of ethanol preference but did no show any altered preference for sweet (saccharin) or bitter (quinine) flavors or change in general caloric intake. These mice were also hypersensitive to the sedating effects of alc. and to the allosteric GABAA agonists pentobarbital and diazepam.

IT **107-35-7**, Taurine
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(altered levels of, in PKC.epsilon. knockout mice; cells and animals deficient in .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics)

RN 107-35-7 CAPLUS

CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1998:621100 CAPLUS
DN 129:239901
TI Anti-epileptogenic agents, and preparation thereof
IN Weaver, Donald F.; Milne, Paul H.; Tan, Christopher Y. K.; Carran, John R.
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9840055	A2	19980917	WO 1998-CA244	19980312
	WO 9840055	A3	19990218		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6306909	B1	20011023	US 1998-41371	19980311
	AU 9864923	A1	19980929	AU 1998-64923	19980312
	EP 969823	A2	20000112	EP 1998-910555	19980312
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	NZ 337849	A	20000128	NZ 1998-337849	19980312
	JP 2001515483	T2	20010918	JP 1998-539010	19980312
	US 2002025949	A1	20020228	US 2001-932676	20010816
PRAI	US 1997-41140P	P	19970312		
	US 1998-73536P	P	19980203		
	US 1998-41371	A3	19980311		
	WO 1998-CA244	W	19980312		

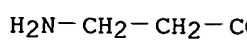
OS MARPAT 129:239901
AB Methods and compds. useful for the inhibition of convulsive disorders, including epilepsy, are disclosed. The methods and compds. of the invention inhibit or prevent ictogenesis and epileptogenesis. Methods for prepg. the compds. of the invention are also described.
IT **107-95-9**, .beta.-Alanine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anti-epileptogenic agents for **convulsive** disorder **treatment**, and prepn. thereof)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

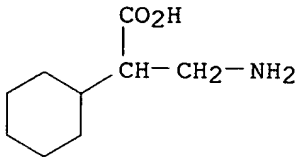
IT **107-95-9DP**, .beta.-Alanine, derivs. **5664-30-2P 213192-48-4P 213192-49-5P 213192-50-8P 213192-76-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anti-epileptogenic agents for **convulsive** disorder **treatment**, and prepn. thereof)

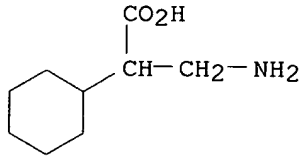
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 5664-30-2 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)- (6CI, 8CI, 9CI) (CA INDEX NAME)

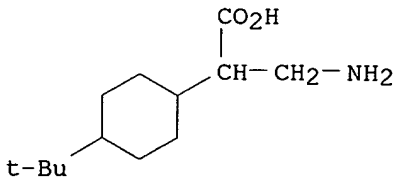


RN 213192-48-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

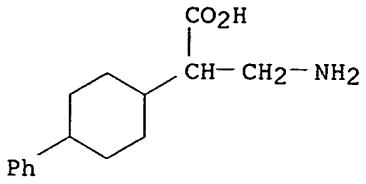
RN 213192-49-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

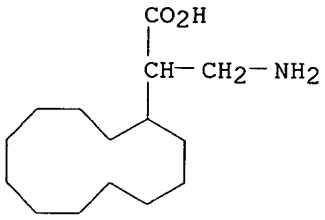
RN 213192-50-8 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl-, hydrochloride

(9CI) (CA INDEX NAME)



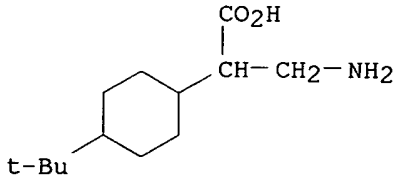
● HCl

RN 213192-76-8 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

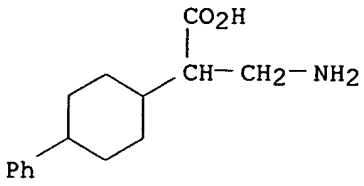


● HCl

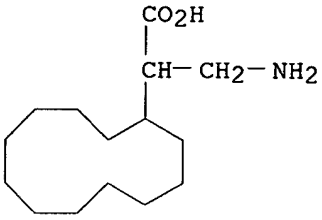
IT **213192-14-4 213192-15-5 213192-16-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-epileptogenic agents for **convulsive** disorder **treatment**, and prepn. thereof)
RN 213192-14-4 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



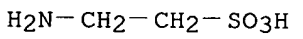
RN 213192-15-5 CAPLUS
CN Cyclohexaneacetic acid, .alpha.-(aminomethyl)-4-phenyl- (9CI) (CA INDEX NAME)



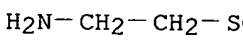
RN 213192-16-6 CAPLUS
CN Cyclododecaneacetic acid, .alpha.-(aminomethyl)- (9CI) (CA INDEX NAME)



L28 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1992:424160 CAPLUS
DN 117:24160
TI Drug-induced seizures in taurine-deficient mice
AU Shimada, Chiaki; Tanaka, Shuichi; Sano, Mitsuo; Araki, Hiromasa
CS Res. Dev. Cent., Fuso Pharm. Ind., Ltd., Osaka, 536, Japan
SO Yakubutsu, Seishin, Kodo (1991), 11(4), 257-60
CODEN: YSKODB; ISSN: 0285-5313
DT Journal
LA Japanese
AB Pentetrazole-, picrotoxin- and strychnine-induced seizures in taurine-deficient mice produced by **treatment** with guanidinoethyl sulfonate (GES), a taurine transport antagonist, were investigated. Mice were fed a taurine-free diet and water contg. 1% GES from 2 wk of pregnancy to weaning. The same feeding condition was applied to male offspring from 3 wk of age. At 5 wk of age, convulsants were administered to some mice and the others were sacrificed for detn. of brain amino acid concns. The incidences of both seizure and death for strychnine and death for picrotoxin were enhanced by **treatment** with GES, whereas the latency of pentetrazole-induced tonic extensor was prolonged. Significant decrease of brain taurine, asparagine and GABA concns. were obsd. in mice **treated** with GES. These results suggest that **convulsive** seizures caused by disinhibition of taurine and GABA system are enhanced by deficiency of brain taurine level.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(deficiency of, seizures induced by GABA or taurine disinhibition enhancement by, amino acids of brain in)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L28 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1989:625241 CAPLUS
DN 111:225241
TI Chronic lithium treatment and status epilepticus induced by lithium and pilocarpine cause selective changes of amino acid concentrations in rat brain regions
AU Jope, Richard S.; Miller, Joanne M.; Ferraro, Thomas N.; Hare, Theodore A.
CS Dep. Pharmacol., Univ. Alabama, Birmingham, AL, 35294, USA
SO Neurochemical Research (1989), 14(9), 829-34
CODEN: NEREDZ; ISSN: 0364-3190
DT Journal
LA English
AB The effects of 4 wk of dietary Li+ **treatment** and of status epilepticus induced by administration of pilocarpine to Li+-**treated** rats were examd. on the concns. of amino acids in 4 regions of rat brain: cerebral cortex, hippocampus, striatum, and substantia nigra. To ensure accurate quantitation of the amino acids, animals were sacrificed by focused beam microwave irradn. and amino acids were measured by using a fully validated triple-column ion-exchanged amino acid analyzer with post-column o-phthalaldehyde derivatization and fluorometric detection. The concns. of 4 amino acids, threonine, methionine, lysine, and tyrosine, were increased in 2-4 brain regions by chronic Li+ **treatment**. Their concns. remained elevated, or were further increased, during status epilepticus. The concns. of 8 amino acids and ammonia were not altered by Li+ **treatment** but increased in concn. during status epilepticus in some brain regions. Glycine, serine, arginine, and citrulline were decreased by chronic Li+ **treatment**. Status epilepticus increased the concns. of these 4 amino acids above that found in the Li+-**treated** samples in some of the brain regions that were examd. Six amino acids and glutathione were generally unaltered by both **treatments**. These results are related to the effects of Li+ **treatment** and are compared with changes reported by others following **treatment** with a variety of **convulsive** stimuli.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, lithium and epilepsy from lithium plus pilocarpine effect on)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L28 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1988:524031 CAPLUS
DN 109:124031
TI Effect of guanidinoethanesulfonate and taurine on convulsions in EL mice
AU Hiramatsu, Midori; Edamatsu, Rei; Kabuto, Hideaki; Kuroda, Munemasa; Mori, Akitane
CS Sch. Med., Okayama Univ., Okayama, 700, Japan
SO Ganryu Aminosan (1987), 10(1), 23-6
CODEN: GAMNDY; ISSN: 0387-6667
DT Journal
LA Japanese
AB Mice were given 1% guanidinoethanesulfonate (I) soln. or 1% taurine (II) soln. as drinking water for 6 mo. In the I-**treated** group, the incidence of convulsions increased throughout the exptl. period from 3 days after starting I **treatment** as compared with that in the control group. 5-HT contents in the cerebral cortex decreased, whereas those in the caudatum, hippocampus, mesencephalone, hypothalamus, pons + medulla oblongata, and cerebellum showed no change. In the II-**treated** group, on the other hand, no change was obsd. in the incidence of convulsions or 5-HT contents in each brain area. The levels of brain free amino acids in the I-**treated** group 3 days after starting of I **treatment** were measured. Glutamate (Glu), alanine, serine, and lysine (Lys) contents in the cerebrum and Glu, Lys, and glycine contents in the cerebellum increased. The increase in **convulsive** sensitivity to I mice is probably due to both decreased 5-HT levels in the cerebral cortex and increased Glu levels in the brain.
IT **107-35-7**, Taurine
RL: BIOL (Biological study)
(of brain, quanidinoethanesulfonate effect on, convulsions in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L28 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1985:199073 CAPLUS
DN 102:199073
TI Effects of glycine and other inhibitory amino acid neurotransmitters on strychnine convulsive threshold in mice
AU Sangiah, Subbiah
CS Coll. Vet. Med., Oklahoma State Univ., Stillwater, OK, 74078, USA
SO Veterinary and Human Toxicology (1985), 27(2), 97-9
CODEN: VHTODE; ISSN: 0145-6296
DT Journal
LA English
AB The effects of glycine [56-40-6] and other inhibitory amino acid neurotransmitters on strychnine (I) [57-24-9] **convulsive** threshold were studied in mice. The mean i.v. threshold dose for I to produce its **convulsive** effects in briefly restrained mice was 1386 mg/kg. The dose of I produced 100% postconvulsive mortality in all the mice tested. I.p. administration of various doses (100-500 mg/kg) of glycine, .beta.-alanine [**107-95-9**], and L-threonine [72-19-5], 15-20 min prior to I infusion, produced an increase of 13.92%, 25.73% and 17.15%, resp., in I **convulsive** threshold in mice. Diazepam [439-14-5], known to produce its anticonvulsant, sedative, and muscle relaxant effects through its interaction either with central GABA or glycine receptors was the most potent (48.39%) in increasing I **convulsive** threshold. Laurine [107-75-5] and Baclofen [1134-47-0] were ineffective in raising I **convulsive** threshold in mice. These observations favor the possible use of either glycine or .beta.-alanine in addn. to diazepam in **treating** clin. cases of I neurotoxicoses.
IT **107-35-7 107-95-9**
RL: BIOL (Biological study)
(strychnine-induced convulsive threshold response to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$

L28 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1984:628789 CAPLUS
DN 101:228789
TI Subcellular distribution of neuroactive amino acids in brains of genetically epileptic rats
AU Bonhaus, Douglas W.; Lippincott, Shirley E.; Huxtable, Ryan J.
CS Health Sci. Cent., Univ. Arizona, Tucson, AZ, USA
SO Epilepsia (1984), 25(5), 564-8
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB The subcellular distribution of amino acids was compared in brains of genetically seizure-susceptible (SS) and genetically seizure-resistant (SR) rats. The total taurine content (.mu.mol/brain) in the P2B, or synaptosomal, fraction in SS rats was only 37% of that of SR rats. Glutamate, glutamine, glycine, alanine, and GABA contents were unaltered. No alterations in total content were found in other subcellular fractions of the amino acids studied. SS animals that had never been stimulated to audiogenic seizure had decreased concns. of taurine (nmol/mg protein) in the P2, P2B, and P2C fractions as compared with SR animals. These fractions contain crude synaptosomes, enriched synaptosomes, and enriched mitochondria, resp. Phosphoethanolamine concns. were also decreased in the P2B fractions, but concns. of other amino acids were unaltered, as compared with SR animals. Twenty-four hours after the intracerebroventricular injection of taurine (6 .mu.mol) in SS animals that had never been convulsed, taurine concns. were increased in whole-brain homogenate and P2 and P2B fractions as compared with SS not given taurine. This **treatment** left unaltered the concns. of glutamate, glutamine, GABA, and glycine in brain homogenate and P2 fraction. Because decreases in taurine concn. were seen in animals that had not been convulsed, these alterations are intrinsic to the SS strain and are not a consequence of **convulsive** activity. In view of the antiepileptic action of taurine, and the fact that an impairment of taurine transport in the brain of SS rats has previously been demonstrated, it is suggested that a defect in the biochem. of taurine is partially responsible for the seizure susceptibility of the SS rat.
IT **107-35-7 1071-23-4**
RL: PROC (Process)
(brain subcellular distribution of, in genetic epilepsy susceptibility)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

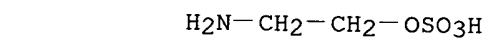
RN 1071-23-4 CAPLUS
CN Ethanol, 2-amino-, dihydrogen phosphate (ester) (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-OPO_3H_2$

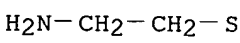
L28 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1982:576457 CAPLUS
DN 97:176457
TI Aspects of the pentylenetetrazol kindling model of epileptogenesis in the rat
AU Fabisiak, J. P.; Schwark, W. S.
CS New York State Coll. Vet. Med., Cornell Univ., Ithaca, NY, 14853, USA
SO Experimental Neurology (1982), 78(1), 7-14
CODEN: EXNEAC; ISSN: 0014-4886
DT Journal
LA English
AB The kindling model of epileptogenesis is characterized by the induction of a persistent redn. of seizure threshold after repeated exposures of the brain to stimuli which were initially subconvulsive. The ability of repeated injections of pentylenetetrazol (PTZ) [54-95-5] to induce kindling was studied. Subconvulsive doses of PTZ (20-25 mg/kg, i.p.) were administered to rats every 4 days for a total of 21 **treatments**. The **convulsive** response score of PTZ-**treated** rats remained elevated upon challenge with 22.5 mg/kg PTZ after a 3-wk PTZ-free period. Studies on the mechanisms involved in PTZ-induced kindling revealed that hepatic microsomal cytochrome P 450 [9035-51-2] concns. were unchanged after chronic PTZ **treatment**. No significant changes in brain amino acids, including GABA [56-12-2] and taurine [**107-35-7**], 2 neuroinhibitory amino acids which have been implicated in the regulation of seizure phenomena, were found in PTZ-kindled animals.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, pentylenetetrazol kindling in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SO_3H$

L28 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1981:132942 CAPLUS
DN 94:132942
TI A comparative study of the pharmacology of inhibitors of GABA-metabolism
AU Loescher, Wolfgang
CS Fachber. Veterinaermed., Freie Univ. Berlin, Berlin, D-1000/33, Fed. Rep. Ger.
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1980), 315(2), 119-28
CODEN: NSAPCC; ISSN: 0028-1298
DT Journal
LA English
AB Gabaculine [59556-29-5], .gamma.-acetylenic GABA [57659-38-8], .gamma.-vinyl GABA [60643-86-9], ethanolamine O-sulfate (EOS) [**926-39-6**], aminooxyacetic acid hemihydrochloride (AOAA) [2921-14-4], Na valproate (VPA) [1069-66-5], and GABA [56-12-2] were studied for anticonvulsant, biochem. and toxic effects in mice. Elevations of the electroconvulsive threshold were produced by the i.p. injection of AOAA, gabaculine, .gamma.-acetylenic GABA, VPA, EOS, .gamma.-vinyl GABA and GABA in decreasing order of potency. All drugs except GABA and VPA increased the clonic pentetrazole threshold to a similar extent, but differed in their increases in the brain content of GABA. The activity of glutamate decarboxylase [9024-58-2]was decreased only by .gamma.-acetylenic GABA. Gabaculine, AOAA, VPA, and in part .gamma.-vinyl GABA and GABA were efficacious enough to allow the detn. of anticonvulsant ED50 values, whereas .gamma.-acetylenic GABA and EOS showed no clear activity in any seizure models used. Gabaculine and AOAA were toxic or lethal. All inhibitors of GABA-.alpha.-oxoglutarate aminotransferase (EC 2.6.1.19) (GABA-T) [9037-67-6]xcept EOS caused numerous side effects which cast doubt on the specificity of these drugs. Apparently, inhibitors of GABA-T are not suited for **treatment** of **convulsive** disorders in humans but are useful tools in studies of exptl. epilepsy.
IT **926-39-6**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pharmacol. and toxicity of)
RN 926-39-6 CAPLUS
CN Ethanol, 2-amino-, hydrogen sulfate (ester) (8CI, 9CI) (CA INDEX NAME)



L28 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1972:560171 CAPLUS
DN 77:160171
TI Amino acids in the cobalt-induced epileptogenic and nonepileptogenic cat's cortex
AU Koyama, Ikuko
CS Dep. Physiol., Univ. Montreal, Montreal, QC, Can.
SO Canadian Journal of Physiology and Pharmacology (1972), 50(8), 740-52
CODEN: CJPPA3; ISSN: 0008-4212
DT Journal
LA English
AB Epileptogenic cortical foci were produced by topical application of cobalt [7440-48-4] powder to the exposed anterior or posterior sigmoid gyrus of adult cats, and within 60-90 min, epileptic discharges were obsd. only in the area adjacent to the Co-**treated** focus. Tonic and clonic epileptic convulsions occurred 24 hr later, but the seizures disappeared by the 3rd day after **treatment**. Concns. of glutamic acid [56-86-0], aspartic acid [56-84-8], and .alpha.-aminobutyric acid [80-60-4] were decreased in the cortical tissue adjacent to the Co application site, and glycine [56-40-6], threonine [72-19-5], serine [56-45-1], and taurine [**107-35-7**] concns. increased markedly during the **convulsive** period. The rate of glutamic acid release increased within 90 min after Co application along with a corresponding decrease of the rate of release of glutamine [56-85-9] and urea [57-13-6]. The excitatory effect of the liberated glutamic acid may be important in the production of focal epileptic discharges following the application of Co powder to the cerebral cortex.
IT **107-35-7**
RL: BIOL (Biological study)
(of brain, cobalt-induced convulsion in relation to)
RN 107-35-7 CAPLUS
CN Ethanesulfonic acid, 2-amino- (9CI) (CA INDEX NAME)



L26 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2003 ACS
AN 1966:62437 CAPLUS
DN 64:62437
OREF 64:11720d-f
TI Anticonvulsive properties of certain .omega.-amino acids
AU Maj, Jerzy; Szurska, Halina; Ostasz, Tadeusz
CS Dept. Pharmacolma., Med. Acad., Lublin, Pol.
SO Dissertationes Pharm. (1965), 17(3), 277-82
DT Journal
LA Polish
AB The anticonvulsive activity of .gamma.-aminobutyric acid, .beta.-alanine, .epsilon.-aminocaproic acid, carnitine, and phenyl-.beta.-alanine was studied in mice. Compds. were given intraperitoneally in doses 0.5 and 1.0 g./kg. in 0.9% saline except for phenyl-.beta.-alanine, which was suspended in 1%, tylose. Intraperitoneal administration of the investigated compds. did not protect against strychnine, cardiazole, megimide, or semicarbazide administered subcutaneously. .gamma.-Aminobutyric acid, and .beta.-alanine given intracerebrally prevented convulsions and death following administration of strychnine. Carnitine did not enhance the **convulsive** and toxic effects of strychnine. Phenyl-.beta.-alanine did not have any effect. The absence of any anticonvulsive effect of .gamma.-aminobutyric acid in semicarbazide intoxication confirms suggestions about the impermeability of the bloodbrain barrier for this compd. 24 references.
IT **107-95-9**, .beta.-Alanine
(antispasmodic activity of)
RN 107-95-9 CAPLUS
CN .beta.-Alanine (6CI, 8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-CO_2H$